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A. M. A. SESSION—San Francisco—JUNE 13-17, 1938

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OTOLARYNGOLOGY IN RELATION TO GENERAL MEDICINE

BURT R. SHURLY, M.D.

DETROIT

This subject was selected from deductions forcibly impressed on me during ten years of experience in examinations of more than 2,300 candidates before the American Board of Otolaryngology. That problems of otolaryngology are clearly related to general medicine has been recognized from time to time in the literature and in practice. The earlier otolaryngologists numbered quite a few men who were trained in general medicine first and in otolaryngology later, whereas the modern specialism concentrates the training for a number of years on otolaryngology and to a considerable extent ignores the related and borderline problems.

Postgraduate instruction in this country is an evolutionary training, and the best opportunities are offered in a comparatively few centers. In the effort to stress the highly technical surgical procedures, the allied specialties, such as neurology and internal medicine, are given scanty consideration. The examinations given by the board indicate that the candidates are splendidly prepared in the diagnosis and treatment of sinus disease, pathologic tonsils and adenoids and in the problems of mastoiditis and understand admirably the treatment of diseases of the throat and acute and chronic suppurative conditions in these localities. But the larynx, the thyroid, infections of the respiratory tract and the problems of internal medicine as related to the ear, nose and throat are passed over with lessened interest and limited knowledge. In order that a model curriculum in graduate and postgraduate study may be attained, a plea is made for broader consideration of the borderline problems and their definite relationship.

The patient now comes to the otolaryngologist more and more frequently through his own choice or through the advice of a friend rather than as a referred patient from the general practitioner. Under the newer psychology, the layman selects his specialist himself; in this he is largely influenced by hearsay evidence of the specialist's ability from various channels of indirect advertising. The information that the certified specialist is especially qualified to treat a particular disease is not yet widely disseminated; it will attain popular understanding within the next decade. The choice of the layman may therefore be erroneous in that he makes his own diagnosis and rushes to the specialist he thinks best fitted to care for his trouble.

Read before the Section on Laryngology, Otology and Rhinology at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1937.

Many acute infections beginning in the nose and throat and ear may become problems of thoracic disease, infection of the brain, arthritis, syphilis, thyroid disease, pneumonia, tuberculosis, furunculosis, cardiac disease, dyscrasia of the blood or an exanthem; therefore a more extensive knowledge than that supplied by a narrow curriculum is essential. The pendulum has swung so far that the otolaryngologist now limits his knowledge and work to the extent that many serious problems associated with the local conditions are in danger of being overlooked without proper investigation. The economic factor also enters into modern medical investigation; the patient finds himself unable to engage from three to five or more specialists to arrive at a correct interpretation of his condition. It is true that the clinic of a large hospital offers a rotating service of cooperation which will cover the individual problem in many cases. It is equally true that not one of these several specialists has either time or opportunity to become personally familiar with the inner life or personal history of the patient who is usually seen for merely a few minutes of examination and observation.

Many cases of pneumonia or tuberculosis in their incipient stages are passed over by the specialist who has no particular interest in diseases of the chest, which extend beyond his field as organized, limited and approved by the general set-up of specialism.

Under the present régime a physician is popularly sanctioned to be an eye, ear, nose and throat specialist, or an ear, nose and throat specialist and bronchoscopist, with full recognition as such. By the same token a man is not expected to be a certificated neurologist, although the specialties of ophthalmology and neurology are intimately related. Certifying boards are not in favor of issuing more than one or at most two certificates to the same person. The requirements for knowledge in the related specialties must therefore be developed in the postgraduate centers of instruction. How much should an otolaryngologist know about borderline medicine and surgery and of those specialties particularly related to his own? Time and convenience have forced an artificial and arbitrary division of disease within limits that are not founded on pathologic consideration. The eye and ear was a specialty of convenience, quite unrelated, in fact, whereas the specialty of respiratory diseases of the nose, throat and chest has much in common, pathologically, bacteriologically and clinically. The latter had a chair in the medical schools of the Mississippi Valley for many years. Ear, nose and throat offer a logical line of work, which has a reasonable basis of association, but, as disease by extension is so frequent, why should the specialist in this line not be interested and trained also in such problems of internal medicine as are found so frequently

on the border line and which exercise such profound influence on diagnosis and therapy in his specialty?

Why should otolaryngology ignore the diagnostic consideration of organic heart disease, cancer, pneumonia, tuberculosis, apoplexy, diseases of early infancy, Bright's disease, diabetes and chronic diseases of the coronary arteries? All these, in the order named (together with violence except suicide), are killing off the race. Cannot otolaryngology lend a helping hand in the detection of the early manifestations of these diseases? Preventive otolaryngology must join hands with internal medicine in a larger way and not remain a trade, with trade restrictions, rules and limitations, that refuses to recognize, in a nonreferred case at any rate, that Bright's disease and diabetes require more for their detection and understanding than they did fifty years ago, when an adequate specimen of urine was sufficient.

While it is true that the laboratory supplies a tremendous number of diagnostic facts and information of great value, the tendency to lean entirely on laboratory reports is responsible for some disasters which combined otolaryngologic and clinical diagnosis might have averted in the earlier stages. The trend has been to throw on laboratory aids the diagnosis of throat conditions. These aids are essential and important, but the divorce of internal medicine from the more highly specialized members of our profession cannot but prove lamentable in the long run. Hypotension and hypertension may be readily measured with a proper blood pressure apparatus and early apoplexy, cardiac change with impending coronary disease, given a better chance of detection.

Pneumonia stands third and tuberculosis seventh in the mortality tables. Will otolaryngology recognize that these death-dealing diseases are frequently extensions or concomitants of infections in the upper respiratory tract and that any good doctor, otolaryngologist or not, should be qualified to diagnose early cases from his own knowledge of physical signs and if necessary call in the internist, the pediatrician, the tuberculosis specialist or the x-ray man if they are available? If not, the otolaryngologist should be considered competent to examine a chest and not have to risk disapproval for not limiting his practice to an artificial boundary above the thyroid cartilages. Who has a better right to be a goiter specialist than a throat specialist, as otolaryngologists are popularly called? The endocrine problem is running away with itself and is in need of reclassification. The diagnosis of hyperthyroidism and hypothyroidism is most intimately connected with otolaryngology; in the sharp limitations of specialism—too sharp, I believe—it has not been considered fashionable or in vogue for the otolaryngologist to know much about the endocrine system. I am of the opinion that he may well include in his equipment a reliable machine for metabolism tests and an allergy set, as they may be valuable aids to therapy.

The otolaryngologist should be ready to give a tuberculin test and refer patients whose reactions are positive for x-ray examination, as many early cases will be discovered if all specialists will be on the alert, especially when dealing with children of high school age. Tuberculosis of the larynx is a later stage of pulmonary tuberculosis, which frequently should have been detected earlier. The fact that tuberculous laryngitis is practically never unaccompanied by pulmonary lesions must be kept constantly in mind. It is only necessary to look back in the literature to the curettage of the larynx, as practiced by Hering and Krause without any regard to the general condition of the patient. Under their leadership, this practice had wide application among laryngologists, and it was some time before it was realized that systemic infection, mixed and tuberculous, was stirred up in many cases. Again, the use of ether narcosis in the presence of active tuberculous laryngitis often adds fuel to the fire. The use of the cautery in the treatment of local lesions of the larynx stands out today as one of the best methods to produce an arrest of the condition. When pulmonary lesions are active, the treatment of the throat must be accompanied by pneumothorax, the crushing or cutting of the phrenic nerve or thoracoplasty, whichever is indicated.

It is important that every laryngologist become a clinician when dealing with tuberculosis. Rest is an essential, as is demonstrated by the rubbing of tuberculous joints, which is done in certain schools of therapeutics. One is confronted with many cases in which the throat apparently has the initial lesion, and the lesion which at the time may be most typical, and is thus easily associated with some other focus of systemic infection. As active tuberculosis may be lighted up by tonsillectomy, especially with the patient under ether anesthesia, a preliminary tuberculin test and x-ray examination are theoretically of service. These tests are practicable occasionally, but, as with some other wise precautions, the cost is often prohibitive. With an alert army of specialists, there is every likelihood that the eradication of tuberculosis would be hastened.

Cancer, closely connected with general medicine and heredity, appears frequently in the otolaryngologist's field, and its early diagnosis is essential to success in treatment. It is second on the mortality table, and one may well examine all older people with that diagnostic possibility ever in mind. Otolaryngologists, familiar with hoarseness as an early symptom, are on guard for the early diagnosis of what quickly becomes a systemic spread of the disease, through the lymphatics, and becomes a general medical problem. Cancer of the throat and of the larynx are continually before the otolaryngologist, and he remains in ignorance of the etiology. Here again, cancer of the throat and general medicine cannot be separated. It is well known that cancer, checked in one locality, may be found a short time later in some other part of the body. The periodic general examination of patients with tuberculosis or cancer is of extreme importance; eternal vigilance is necessary for the detection of recurring lesions. The invasion of the ear, nose and throat with acute or chronic focal infection is a subject well understood, and yet the ravages of Streptococcus viridans or Streptococcus haemolyticus, as they invade the endocardium, the joints and other parts of the body, are problems of general medicine.

The reawakening to the importance of the eradication of syphilis, said to affect one out of four of the human race, must necessarily interest the otolaryngologist and the internist. Physicians are in the throes of a great crusade to uncover syphilis and to make the public more open minded in the discussion and understanding of this disease. The otolaryngologist, from the earliest origin of the specialty, has detected primary and secondary lesions. Every hospital could cooperate in the present campaign by having a Wassermann or a Kahn test performed on every patient when admitted.

A routine blood test on all patients and a test of the spinal fluid when necessary will prove valuable. It has been my practice for some years to make a blood test

on every candidate for operation on the nose or throat, and the positive reactions have a surprising occurrence in totally unexpected cases. This test, before a submucous operation, is a protection to the patient and the physician, and the same rule holds good for all operative work that does not fall within the realm of emergency operating. While it is true that under the modern system of therapeutics the tertiary lesions of syphilis, as found in the mediastinum, the lymphatic glands and the nervous system, have diminished, it is only fair to the patient that any infection of syphilis, so readily determined, should not be overlooked. If otolaryngologists are to join in eliminating the ravages of syphilis and in promoting the proper prophylactic measures, Kahn and Wassermann tests must ultimately be made a routine procedure. If the cost of the examination is beyond the financial means of the patient, I believe the department of health should take care of this contagious disease. If this is state medicine, I am for that much of it—to carry preventive medicine into the field of public protection.

It is a simple matter for one who delves in surgery exclusively to become a therapeutic nihilist and scorn the various therapeutic measures that have stood the test of time and practice. The many examinations conducted by the American Board of Otolaryngology show that the importance of pulse, temperature and respiration is too often disregarded. The consideration of the patient as a psychologic unit, as a member of the human family, with the tremendously influential hysterical, psychic, emotional and hereditary factors, may be lost in the study of the case. The anxiety to demonstrate pathologic tonsils, sinus infection, acute mastoiditis and the necessity of operation may sometimes cause the otolaryngologist to ignore the underlying peculiarities of the individual patient. This fact is elementary, but in all clinics or hospitals eternal vigilance is necessary to uncover all possible disease at the onset.

Preventive and general medicine, with dermatology and otolaryngology, can work together to advantage in this regard. The century-old practice of clinical medicine cannot be separated completely from otolaryngology. The latter evolved from general medicine, separated rapidly under the enormous demands for greater skill in technic, and yet the cycle cannot be completed until the pendulum swings back, as it must in all great movements, to its proper place, and fair consideration is given to all the various scientific facts which influence both the diagnosis and the treatment.

The American Board of Otolaryngology recognizes that the specialty cannot be practiced exclusively but that a 10 to 20 per cent margin for borderline work and related general problems is admissible.

62 West Adams Street.

ABSTRACT OF DISCUSSION

DR. FRANK R. SPENCER, Boulder, Colo.: One hears occasionally of primary laryngeal tuberculosis, the diagnosis having been made without a thorough physical examination and an x-ray examination of the chest. Stubborn diseases of the ears, nose and throat may be much less obscure after a Wassermann test. A biopsy may decide whether a tumor is benign or malignant, and the degree of malignancy according to Broder's classification. The etiology of a paresis or paralysis of the recurrent laryngeal nerve can rarely be determined by the laryngologist. The internist is needed. Fürstenberg's recent article shows the importance of intracranial lesions in the etiology particularly of unilateral laryngeal paralyses and the help that may be rendered by the neurologist. Recently I saw a patient who lost 18 pounds (8 Kg.) after the successful removal of a malignant tumor. A thorough reexamination and urinalysis showed that he had diabetes. With a proper diet and insulin he has improved rapidly. The malignant tumor was properly diagnosed and removed with an excellent result. The diabetes was not even suspected by the clinical laboratory in an excellent hospital. This will also show that mistakes may be made on either side. In the West we see patients with a diagnosis of pulmonary tuberculosis, when the correct diagnosis of bronchiectasis should have been made. This is important because so many patients have sinus disease causing the bronchiectasis. Dr. Shurly wants otolaryngologists to think of patients in terms of other organs and other diseases. He wants to see specialists broadly trained. The eagerness with which younger otolaryngologists are seeking graduate courses at the annual meetings of the Academy and their desire to know more about gross and microscopic pathologic changes are very encouraging signs of the times and lead all of us to believe that Dr. Shurly will realize his ambition.

DR. W. P. WHERRY, Omaha: It is customary to classify medical students as being in the upper, middle or lower third of the class and efficiency graphs are drawn by groups. If it were possible to classify practitioners of medicine in the same manner, the errors herein summarized as a graph of the specialty as a whole might fall in the group constituting the lower two thirds. The records now being accumulated by various examining boards will, I am sure, corroborate this assumption. The evaluation of general medicine and of otolaryngology are but a partial yardstick of usable knowledge—the full yardstick is determined by (1) the training background and (2) that innate urge in some to look on this training factor as only an introduction to the threshold of knowledge. In this connection, in the past twelve years it has been my privilege to analyze the results of examination and credential records of 2,400 candidates appearing before the Board of Otolaryngology. I have been impressed with figures showing the groups having the least failure percentage; namely, the three, four and five year residences and the assistant trained divisions. I question whether Dr. Shurly, in his analysis of otolaryngologists as a whole, has considered the better trained group. Perhaps as the poorer trained sections are eliminated from the scheme of graduate education the graph of otolaryngology (now seemingly dominant) will be redrawn to a higher level. In other words, the answer to Dr. Shurly's inquiry lies in a consistent program of increasing training facilities, bettering the graduate student output by circumscribing the acceptance into the specialty of those poorly trained.

DR. CLAUDE P. BROWN, Philadelphia: One of the difficulties experienced by the clinical pathologists has been due to the physician selecting such examinations as are in agreement with his clinical experience. Nevertheless there is a definite trend to call the clinical pathologist as a consultant and such examinations are made as he considers essential. Bacteriologic examinations supplementing blood examinations certainly are worth while. Normally there may be no bacteria or only a few staphylococci, as the nasal secretions are bacteriostatic. When streptococci, pneumococci or Staphylococcus aureus are present they are of great clinical importance. Throat cultures of normal patients often show streptococci, usually of the viridans type, Staphylococcus albus and Micrococcus catarrhalis, less frequently pneumococci, hemolytic streptococci and Staphylococcus aureus, the latter three frequently pointing to definite infection. As otolaryngology finds itself requiring more training in general medicine, so must it also depend on clinical pathology for blood, bacteriologic, serologic and chemical studies and their interpretation. Some otolaryngologists will no doubt be interested in the use of vaccine in ear and sinus infections due to type III pneumococcus. As reported by Dr. Goldman, I would suggest that the bacteriologist use broth of from 0.1 to 0.2 per cent instead of 1 per cent dextrose, because the acid produced in the latter will kill the pneumococcus before maximum growth occurs; also that an eighteen hour period be the time limit. The smears should show mostly gram-positive organisms and, if not, even a shorter period of growth should be used, other-

wise maximum immunizing effects will not result from the use of the vaccines. I would make a plea for wider use of vaccines. If vaccines are prepared from organisms such as pneumococci, kept virulent by animal (mouse) passage, no one needs to be much troubled, because the same results will be obtained as if they were prepared directly from the patients' cultures.

DR. CHARLES L. BROWN, Philadelphia: I feel that Dr. Shurly's paper is most important and especially significant at this time. There have been numerous references throughout the paper and the attendant discussions indicating the importance of adequate special and general training after graduation from the medical school, and also there have been pointed out a lesser number of so-called failures among those men who have been so trained. As Dr. Shurly's paper has brought out the comprehensive correlation of internal medicine with otolaryngology, it behooves internists to try to provide the type of training that has been anticipated in the words given by the speakers here. I feel that internists have a difficult problem in doing that. The man seeking qualification in otolaryngology does not wish nor does it seem necessary for him to spend an extensive amount of time in an appointment in internal medicine. Yet in the ordinary hospital organization it is difficult to offer training in internal medicine and nose and throat work at the same time, unless some liaison is established between these two departments. The rotating internship has made this possible in a measure but is unsatisfactory because of the short period of service, it being more adequately accomplished in the two year rotating internship with at least a six months service in medicine. Many of us in institutions are confronted with the problem of providing adequate training for internists as required by the Board of Certification. Since the goal of the majority is the practice of medicine there is merit to a three year plan in which the first year after internship is largely clinical, the second year largely investigative and for special study in the fundamental sciences, allied with medicine, and the third year again largely clinical, the principles learned in the two previous years being applied just before one anchors oneself in practice. Possibly some such arrangement as that might be very valuable in the training of the otolaryngologist, and during this intermediary year a part of the time could be given over to a liaison with the department of internal medicine.

DR. BURT R. SHURLY, Detroit: I enjoyed the discussion, which to me means that we have a point of view in orienting and coordinating and trying to reach the proper zenith of postgraduate study in this country, so that a sane, common-sense arrangement can be made whereby our younger men will be broadened and made familiar with those essentials that are destroying the race. If one examines the mortality, heart disease is first, cancer is second and pneumonia third or fourth, while tuberculosis has been put down from the first to the seventh place. Are not those the things for all specialists to be thoroughly familiar with in their early diagnosis, no matter whether one turns the case over to an internist or not? The plea is for the early detection of those diseases related to the ear, nose and throat, focal infection, with heart disease, that are destroying the race, because petrositis, with all due respect to the wonderful research work that has been done, is just an occasional case, compared with the dire death-dealing results of heart disease and pneumonia in our country.

One Rudimentary Sphenoid Sinus.—The sphenoid sinus is an extremely variable cuboidal cavity occupying the body of the bone. Its development begins at the third month of fetal life and is complete at puberty. The two sides rarely develop symmetrically and it is not uncommon to find one sinus rudimentary while its fellow on the opposite side invades the greater and lesser wings of the sphenoid and pneumatizes the pterygoid process. The average adult sinus has six surfaces, the anterior, posterior, superior, inferior, medial and lateral. The thickness of the walls depends upon development of the sinus, a half millimeter being the average measurement of the fully developed wall.—Dixon, F. W.: LVIII. A Comparative Study of the Sphenoid Sinus (A Study of 1,600 Skulls), *Ann. Otol. Rhin. & Laryng.* **46**:687 (Sept.) 1937.

OBSERVATIONS ON ACACIA THERAPY IN NEPHROSIS

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The use of acacia in the symptomatic treatment of nephrotic edema is based on sound physiologic principles, since this particular form of edema is associated directly with massive albuminuria and conspicuous reduction of the concentration of protein in the circulating blood plasma. The lowered colloid osmotic pressure of the blood disturbs the normal mechanism by which fluid is transported and distributed throughout the body. The resulting massive and persistent anasarca often resists the action of the usual diuretics and renders the chronically nephrotic patient especially subject to streptococcic or pneumococcic infection.

The cause of the hypoproteinemia is not definitely known; it is generally supposed, however, to result from defective formation of protein associated with conspicuous loss of protein in the urine. Theoretically the frequent transfusion of plasma or whole blood is the best form of replacement therapy and is sometimes practicable in treating children. In the treatment of adults, however, when from 20 to 30 Gm. of protein is being lost daily in the urine, the protein that can be added in a 500 cc. transfusion may be completely excreted within twelve to forty-eight hours. Therefore attention has been directed toward the use of acacia, a colloid which is able to replace temporarily the lacking plasma protein.

Although the intravenous injection of acacia solution had been used for many years as a substitute for blood transfusion in shock or hemorrhage, its application to the treatment of nephrotic edema began with a study by Hartmann and Senn [1] in 1932. Clinical observations have shown that the injection of acacia is not entirely without danger. Austin and McGuinness [2] reported an alarming increase in blood volume following a single large injection. Maytum and Magath [3] raised the question of possible anaphylactic reactions. Undesirable deposition of acacia in the liver has been described by Dick, Warweg and Andersch.[4]

Nevertheless, further studies on acacia therapy in adults seemed desirable owing to the occasionally striking relief of otherwise intractable anasarca. The rapid disappearance of nephrotic edema and subsequently decreased albuminuria and cast excretion led to the suggestion in some clinical reports [5] that acacia may at times hasten healing of the renal lesion in addition to its purely physical action on the movement of fluid from the tissue spaces to the blood stream. The direct effects of acacia therapy on albuminuria, cylindruria and hematuria in renal disease have so far not been studied in detail. The observations to be reported concern them-

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From the Departments of Medicine and Pharmacology, University of Pennsylvania School of Medicine. The expenses of these studies were in large part defrayed from a grant by the Commonwealth Fund.

1. Hartmann, A. F., and Senn, M. J. A.: Studies in Edema, with Particular Reference to the Therapeutic Value of Acacia, Tr. Am. Pediat. Soc. **44**: 56, 1932.
2. Austin, J. H., and McGuinness, A. C.: A Precaution Concerning the Treatment of Edema by Intravenous Administration of Acacia, Tr. A. Am. Physicians **48**: 276, 1933.
3. Maytum, C. K., and Magath, T. B.: Sensitivity to Acacia, J. A. M. A. **99**: 2251 (Dec. 31) 1932.
4. Dick, M. W.; Warweg, Edna, and Andersch, Marie: Acacia in the Treatment of Nephrosis, J. A. M. A. **105**: 654 (Aug. 31) 1935.
5. Barch, J. H., and Boyd, D. M.: Hypoproteinemic Nephrosis and Its Treatment with Acacia, Am. J. M. Sc. **189**: 536 (April) 1935. Hartmann and Senn.[1]

selves primarily with Addis counts of the urinary sediment before, during and after the injection of acacia in relatively small repeated doses.

Acacia was administered to six patients with nephrotic anasarca and, in far smaller dosage, to two patients with mild glomerulonephritis but no edema. Of the six patients with anasarca, two presented the typical picture of lipoid nephrosis without clinical or urinary evidence of glomerulonephritis. One patient had amyloid nephrosis and in three the nephrotic syndrome appeared in the course of early subacute glomerulonephritis with microscopic hematuria, very slightly diminished kidney function, at most a minor and transient nitrogen retention, little or no hypertension, and no cardiac involvement.

METHODS

For some days or weeks prior to the institution of acacia therapy, the edematous patients had been on a salt poor, high protein, high caloric diet for the most part under close supervision in a metabolic ward. Fluid intake was restricted and in five instances numerous diuretics had been tried without success. The blood pressure was taken twice daily. Twenty-four hour urine specimens were collected continuously. Fluid intake was kept constant so that, except during diuresis, large changes in specific gravity might be avoided. Albuminuria and chloride excretion were determined daily. By means of the Addis technic the excretion of casts, erythrocytes and leukocytes was estimated at frequent intervals. Urea clearances were determined daily over twenty-four hour periods, as described in a previous paper.[6] Preliminary skin tests for sensitivity to acacia were negative in all six patients. Commercial 30 per cent acacia was diluted with four parts of distilled water, so that the fluid injected intravenously contained 6 per cent acacia in 0.9 per cent sodium chloride solution. After an initial test dose of from 5 to 10 Gm., subsequent daily doses ranged from 20 to 30 Gm. until a total of from 120 to 180 Gm. had been given over periods ranging from six to nine days. In agreement with the experience of others, it was found that reactions occurred occasionally unless the undiluted solution as supplied commercially was clear and yellow, or at most light amber, in color. Very slow intravenous injection and the administration of amytal or morphine seemed to assist in avoiding reactions.

OBSERVATIONS

The daily injection of from 20 to 30 Gm. of acacia (in conjunction with restriction of fluid and salt) produced a satisfactory diuresis and temporary freedom from edema in five of the six cases of nephrotic anasarca. In one case the injection of 140 Gm. over a period of six days produced by itself no significant diuresis, but the subsequent administration of theophylline with ethylenediamine, U. S. P. (aminophylline) was followed by a copious diuresis, although the latter drug when used prior to acacia therapy had not affected the flow of urine appreciably.

The excretion of chloride in the urine, usually less than 1 Gm. in twenty-four hours in patients with nephrotic anasarca, increased temporarily during acacia diuresis to as much as 18 Gm. daily. The total amount of chloride excreted during the period of weight loss was roughly equal to the amount of chloride in the injected acacia solution (4.5 Gm. of sodium chloride for each 30 Gm. of acacia) plus that of the excreted edema fluid. When diuresis ceased, chloride excretion again returned to its previous low level until dietary salt restriction was made less rigid. The blood pressure was normal, or slightly below normal, in four cases; in two cases, both of subacute glomerulonephritis, the systolic blood pressure was never above 150 mm. of mercury. The daily injection of 20 to 30 Gm. of acacia did not elevate blood pressure measurably. This contrasts with the effect of a single large dose, which can produce an alarming transient hypertension.[2]

In none of the six cases was there any clear evidence that the administration of acacia affected hematuria, cylindruria or albuminuria significantly. Chart 1 summarizes observations, characteristic of the group, made during the treatment of a woman, aged 27, with a typical initial attack of lipoid nephrosis without clinical evidence of glomerulonephritis. On admission the patient presented massive peripheral edema, pleural effusion and ascites. The body weight ranged from 165 to 170 pounds (75 to 77 Kg.), approximately 30 pounds

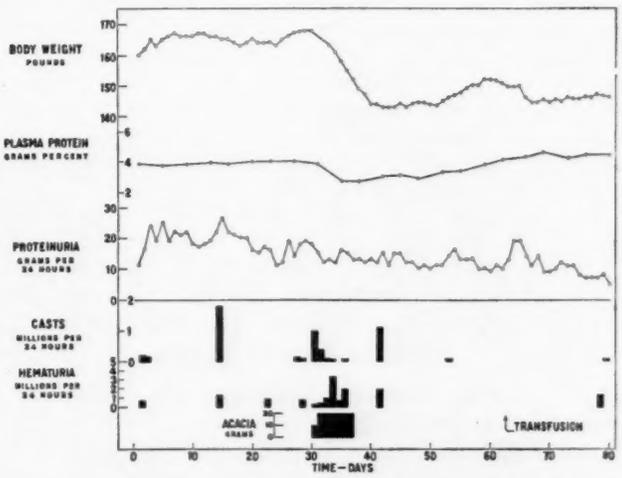

Chart 1.—Effect of acacia on body weight, plasma protein percentage, proteinuria and urinary sediment of a patient with lipoid nephrosis.

(13.6 Kg.) above her normal weight. The urinary output was less than 200 cc. in twenty-four hours. The blood cholesterol was over 600 mg. per hundred cubic centimeters and the urine contained doubly refractile lipoid bodies. The blood pressure, urea clearance and blood urea nitrogen were normal. As shown to the left in chart 1, the proteinuria ranged from 11 to 27 Gm. in twenty-four hours, with a plasma protein concentration of 3.8 Gm. per hundred cubic centimeters. Approximately 200,000 casts and 0.7 million red cells were excreted in twenty-four hours.

A diet high in protein and total calories, but low in salt and fluid content, was given continuously throughout the period of hospitalization. During the first thirty days ammonium chloride, thyroid substance and urea in full dosage failed to affect the body weight appreciably. A small area of cellulitis then developed in the right lumbar region. Fear that this infection might spread led to the administration of acacia.

After sensitivity had been excluded, an initial dose of 10 Gm. was followed by 20 Gm. daily (as shown at bottom of chart 1) until a total of 130 Gm. had been injected over a period of seven days. A satisfactory diuresis followed and body weight decreased by 24 pounds (11 Kg.) in ten days. Simultaneously, with the onset of diuresis, the plasma protein percentage fell

6. Landis, E. M.; Elsom, K. A.; Bott, P. A., and Shiels, E. H.: Observations on Sodium Chloride Restriction and Urea Clearance in Renal Insufficiency, J. Clin. Investigation **14**: 525 (Sept.) 1935.

rapidly from 4.0 to 2.9 Gm. per hundred cubic centimeters and then rose slowly after the end of diuresis to reach 4.1 within thirty days after the injection of acacia was started. Proteinuria, which on admission had been as high as 25 Gm. in twenty-four hours, was slightly less than 10 Gm. in twenty-four hours on discharge, having decreased slowly and regularly without showing any change that could be referred to acacia therapy (chart 1). The excretion of casts and erythrocytes was not modified in any striking manner during or after acacia therapy. Erythrocyte excretion may have increased slightly and temporarily during the diuresis, but the change was not great and, in any event, did not persist after the diuresis was complete. Blood pressure, blood urea nitrogen and urea clearance (not charted) also showed no significant change during or after acacia therapy.

The effects of acacia were temporary in that fluid reaccumulated unless the plasma protein approached the normal level shortly after diuresis ceased. Thus, as shown in chart 1, the body weight began to increase slowly twenty days after diuresis ended. At this point a blood transfusion was followed by renewed diuresis and the slight residual peripheral edema disappeared. The patient, whose urinary signs persisted, was discharged on a diet high in protein, total calories and vitamins. Edema did not recur, the plasma protein percentage returned to normal and one year later the urine was normal by Addis count and there were no signs of an active renal lesion.

That acacia therapy affects the fluid balance only temporarily is illustrated also by the tendency for edema to return after weeks or months, as the disease again becomes active. One patient, described in full elsewhere,[7] suffered from subacute glomerulonephritis in the course of which four major attacks of nephrotic

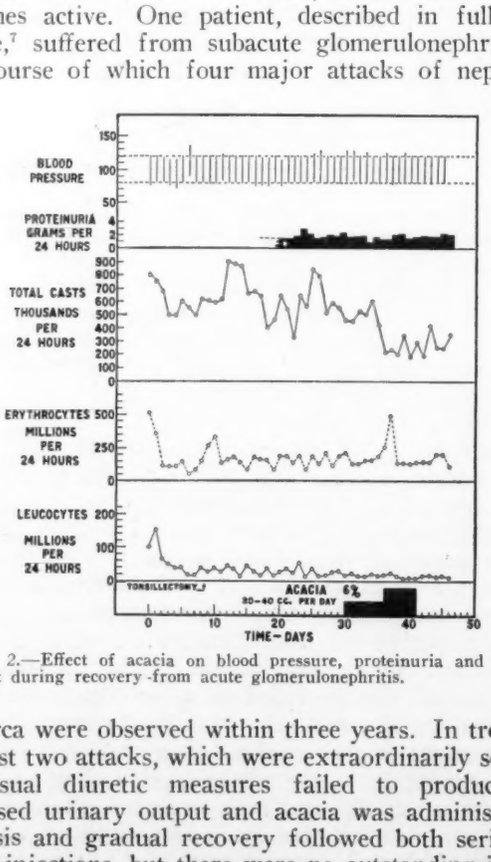
BLOOD PRESSURE
PROTEINURIA GRAMS PER 24 HOURS
TOTAL CASTS THOUSANDS PER 24 HOURS
ERYTHROCYTES MILLIONS PER 24 HOURS
LEUCOCYTES MILLIONS PER 24 HOURS
TONSILLECTOMY
ACACIA 6% 30-40 CC. PER DAY
TIME - DAYS

Chart 2.—Effect of acacia on blood pressure, proteinuria and urinary sediment during recovery from acute glomerulonephritis.

anasarca were observed within three years. In treating the first two attacks, which were extraordinarily severe, the usual diuretic measures failed to produce an increased urinary output and acacia was administered. Diuresis and gradual recovery followed both series of acacia injections, but there were no outstanding immediate effects on the urinary signs. Moreover, the injection of acacia did not protect against relapse. The third and fourth attacks of edema in this patient were associated with milder grades of hypoproteinemia and were relieved simply by salt restriction and purine diuretics. The renal lesion, in this case a definite glomerulonephritis, remained intermittently active after both injections of acacia. As in the other cases studied, although diuresis was induced there was no evidence from cast counts that the acacia had affected the underlying renal lesion either beneficially or deleteriously.

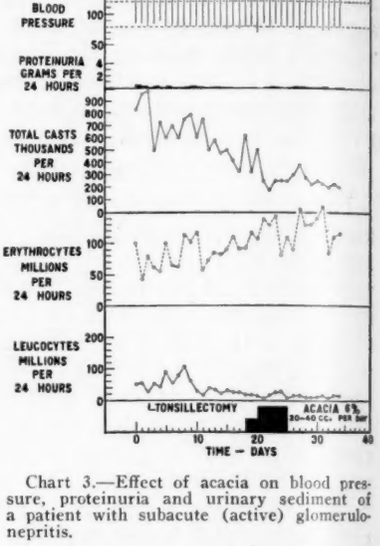

Chart 3.—Effect of acacia on blood pressure, proteinuria and urinary sediment of a patient with subacute (active) glomerulonepritis.

It has been known for some time that acacia modifies the properties of the circulating erythrocytes, the surfaces of which are presumably coated by adsorption. The sedimentation rate is increased,[8] oxygen combining power is modified,[9] and hemolysis becomes more difficult.[10] It seemed possible that adsorption of acacia by renal cells or capillaries might in some way modify the character of the urinary sediment. Therefore, small amounts of acacia were administered to two patients with renal disease but without edema, to study the possible effect on hematuria, albuminuria and cylindruria uncomplicated by diuresis.

Chart 2 summarizes an observation on a patient recovering from acute glomerulonephritis. The blood pressure, originally elevated, had been normal for a period of two weeks before the observations were begun. Tonsillectomy was performed on the ninth day, as shown at the bottom of the chart. Acacia in doses of from 2 to 3 Gm. was given daily for eleven days. These injections had no demonstrable effect on the blood pressure, proteinuria, cylindruria, hematuria or leukocyte excretion. So far as could be ascertained, the added colloid passed through the kidneys as an inert foreign body. Similar results were obtained in a patient with active subacute glomerulonephritis, as shown in chart 3. Again the repeated administration of acacia in small doses did not modify blood pressure or the excretion of formed elements in the urine.

COMMENT

Amberson[11] has demonstrated the degree to which acacia may take the place of plasma proteins. In dogs it has been possible to reduce the concentration of the plasma proteins to 0.05 per cent by repeated plasmapheresis, provided the removed plasma was replaced by 6 per cent acacia in physiologic salt solution. The animals remained in good condition and showed at

7. Landis, E. M., and Elsom, K. A.: The Nephrotic Syndrome in Adults, Internat. Clin. **1**: 1 (March) 1937.

8. Lucia, S. P., and Brown, J. W.: Suspension Stability of Erythrocytes in Solutions of Gum Acacia, Proc. Soc. Exper. Biol. & Med. **32**: 189 (Oct.) 1934.

9. Christie, A.; Phatak, N. M., and Olney, Mary B.: Effect of Intravenous Acacia on Physiochemical Properties of the Blood, Proc. Soc. Exper. Biol. & Med. **32**: 670 (Feb.) 1935.

10. Walker, M. A.: Tenth-Normal Hydrochloride Acid as Diluent for Counting Leukocytes After Infusion of Solution of Acacia, Am. J. Clin. Path. **2**: 347 (July) 1932.

11. Amberson, W. R.: Blood Substitutes, Biol. Rev. **12**: 48, 1937.

most slight edema. In treating nephrotic children, Hartmann and Senn [1] advocated the use of relatively large doses of acacia, namely, from 1 to 2 Gm. per kilogram of ideal body weight, repeated if necessary. By calculation this dose should raise the colloid osmotic pressure of the blood to 17 cm. of water—the so-called edema level. Austin and McGuinness,[2] however, observed a dangerous increase in blood volume when this dosage was used in a young adult and suggested that acacia induces diuresis primarily by withdrawing fluid from the edematous tissues and increasing blood volume temporarily. If this is true, diuresis might occur with doses considerably smaller than those advocated by Hartmann.

The observations here reported are in accord with this interpretation in that significant diuresis sometimes began as early as the third or fourth day after only 60 to 80 Gm. of acacia had been given. Even if increase in blood volume and loss of acacia from the blood stream are left out of account, this dose would be too small to raise the colloid osmotic pressure of the blood to the "edema level." Rapid decrease of plasma protein concentration and hemoglobin percentage provide additional indirect evidence that blood volume was increased by relatively small doses of acacia.

In these observations acacia was used only in association with rigid salt restriction, which may have increased the effectiveness of the added colloid to some extent. Synergistic action between acacia and the ordinary diuretics seems possible. In one case theophylline with ethylenediamine, U. S. P., used alone produced no diuresis. Subsequently, after 140 Gm. of acacia had been injected without response, the administration of theophylline with ethylenediamine, U. S. P., in the same dosage was followed by a copious diuresis. It is possible that small doses of acacia, in combination with other diuretics, will prove more reliable and less dangerous than large doses of acacia alone. Definite evidence on this point is, however, still lacking.

The cautious administration of acacia by repeated daily injections of from 20 to 30 Gm. appears to be relatively safe and, in combination with salt restriction, has induced diuresis even when the plasma proteins were extremely low. The failure to observe any effect, irritative or curative, on the renal lesion itself agrees with the conclusions of Huffman,[12] who made routine urine studies before and after acacia was administered for hemorrhage and shock in patients without primary renal disease. The colloid is apparently excreted as an inert foreign body even by the diseased kidney, its only effect being the physical one of inducing diuresis when the colloid is present in the blood in sufficient concentration. According to Dick and his associates,[4] the use of acacia in very large amounts does not raise the blood level in proportion to the dose, because as the concentration of acacia in the blood approaches a certain maximum, which may vary from one person to another, the excess acacia is merely stored in the tissues. Repeated administration of small doses makes it possible to limit the total amount given if diuresis appears early and to discontinue injections if undesirable effects are observed. The danger of suddenly increasing blood volume is avoided and there is time for adaptation. It is probable that, if diuresis has not begun by the time 150 Gm. has been given to an adult, little is to be gained by administering larger doses.

12. Huffman, L. D.: Solution of Acacia and Sodium Chloride in Hemorrhage and Shock, J. A. M. A. **93**: 1696 (Nov. 30) 1929.

In treating nephrotic edema, the usual diuretics should be tried first, since they are in general less apt to produce undesirable side effects. Acacia was given to our six patients for definite indications. In one case it was used because of a threatening skin infection, other diuretics having been tried without success. In the others, rapidly increasing anasarca resisted other therapy and rendered it imperative to induce diuresis promptly or else resort to mechanical drainage or to one of the mercurial diuretics. It is generally agreed that mechanical drainage is hazardous owing to the greater danger of infection in nephrotic patients. Opinion is divided concerning the desirability of using mercurial diuretics in treating a condition characterized by conspicuous tubular degeneration.

The permanent relief of nephrotic edema depends, of course, on the rate at which plasma proteins are formed and the rate at which protein is lost in the urine. According to available evidence, persisting improvement after acacia therapy cannot be ascribed to any specific effect of the colloid itself on the renal lesion. Relief of edema does, however, reduce the danger of infection and may favor the development of a spontaneous remission by relieving the anorexia and the gastro-intestinal disturbances that accompany persistent ascites.

SUMMARY

Acacia was administered in repeated daily doses of not more than 30 Gm. to six patients with nephrotic edema, the total dosage being 180 Gm. or less. In combination with a low fluid intake and rigid salt restriction, acacia produced a satisfactory diuresis in five of the six patients. In one patient acacia per se failed to induce diuresis but apparently increased the effectiveness of theophylline with ethylenediamine, U. S. P., as a diuretic.

Repeated Addis counts of the urinary sediment before, during and after the administration of acacia did not reveal any definite beneficial or deleterious action of this substance on the underlying renal lesion.

Small daily doses of acacia have so far not produced any change in blood pressure or any dangerous increase in blood volume. Though its diuretic effect is only symptomatic and temporary, acacia has been useful in treating persisting nephrotic edema in patients with marked hypoproteinemia, provided renal insufficiency, hypertension and cardiac failure are not complicating factors.

Before acacia is used, patients should be tested carefully for sensitivity. The total dose should be kept below the level at which marked deposition in tissues occurs. Undoubtedly the ordinary diuretic drugs are preferable if they are efficacious and acacia should be reserved for persistent, severe nephrotic edema that has, by test, resisted other therapy. In such selected cases acacia frequently provides symptomatic relief otherwise unobtainable and also assists in avoiding the dangerous infections to which patients with persisting nephrotic edema are subject.

ABSTRACT OF DISCUSSION

DR. A. R. BARNES, Rochester, Minn.: Ever since Hartman in 1933 introduced the use of acacia in cases of edema with hypoproteinemia, it has constituted a valuable adjunct to treatment in these cases. Hartman and Landis pointed out that other diuretic measures should be given a thorough trial first. In the original recommendation Hartman suggested the administration of enough acacia to raise the osmotic pressure to about the normal level. According to my experience, such

large doses have not been necessary, because I have found, as Dr. Landis has shown here, that when the acacia treatment of this type of edema is successful the response is obtained from smaller doses. Binger and Goudsmith in the last few weeks have studied two cases which raised two interesting questions. These were both cases of lipemic hypoproteinemic edema. Both patients were carefully treated over a sufficient period with the usual diuretic measures, including a high protein diet, salt restriction, administration of salyrgan, administration of large amounts of potassium nitrate and raising the basal metabolic rate, without securing successful diuresis. The patients were then given acacia intravenously in a dose ranging from 1.5 to 2 Gm. per kilogram of body weight. This resulted in a concentration of acacia in the blood of one of these patients of 0.6 Gm. per hundred cubic centimeters. Following the administration of acacia in these amounts, a very slight diuresis was obtained. The day following the administration of the acacia, the patients were given salyrgan intravenously, which resulted in very satisfactory diuresis. The fact that satisfactory diuresis is obtained from smaller doses of acacia than those sufficient to bring the osmotic pressure to normal, and the experience that sometimes when one brings up the osmotic pressure satisfactory diuresis depends on the administration of additional diuretics, suggest that there are some factors in the production of diuresis other than the mere raising of osmotic pressure. As Amberson has shown, acacia administered intravenously is the most satisfactory artificial substitute for plasma. According to my experience, if carefully prepared and carefully administered, the drug can be given without untoward results. This presentation teaches us that we may obtain results from much smaller doses. It is a valuable contribution to the treatment of edema associated with hypoproteinemia.

THE PREVENTION AND MODIFICATION OF MEASLES

CHARLES F. McKHANN, M.D.
BOSTON

Sizable decreases have taken place in recent years in the incidence of certain communicable diseases, notably enteric infections, tuberculosis and diphtheria; the incidence of other diseases, among them measles, has remained unchanged. Public health measures for the control of measles have been entirely inadequate. No satisfactory means of active immunization has been developed; isolation of patients, placarding of homes and closing of schools have had no appreciable influence on the control of outbreaks of the disease. Nevertheless, the death rate from measles has shown a steady decline, as exemplified by the figures for Massachusetts for the years 1920 to 1936 (table 1).

The diminution in deaths from measles may be due in part to the recognition that the disease is particularly dangerous in children of preschool age and that, although almost all persons sooner or later acquire measles, needless exposure, particularly of small children, is unwarranted and should if possible be avoided. Reduction in the death rate may be further attributed to the wider recognition of the desirability of isolating patients with measles one from another. In years past it was customary in hospitals to segregate children with measles in large wards for group isolation on the basis that they could not transmit the disease to one another. However, patient A would be a carrier of a pneumococcus and patient B would be a carrier of a streptococcus, and, although it is true that they could not infect each other with measles, they could interchange their usual pharyngeal organisms. In homes, institutions and hospitals where patients with measles have been isolated individually, secondary infections of the respiratory tract have been noticeably less frequent.

The reduction in the incidence of nutritional disorders and deficiency diseases in children, together with improvement in housing conditions as well as extensive progress of child welfare work, has reduced the number of chronically ill, debilitated children, in whom measles found many of its victims.

Long time surveys of disease lead to the conclusion that the severity of certain infections runs in waves dependent in part on the diminished resistance of populations but also on unexplained variations in the virulence of the virus. That fluctuations in mass resistance to measles have been of some importance in the past is shown by descriptions of the severe forms of measles observed in countries and communities from which the disease had long been absent. The theory that it is the current recognition of the dangers of measles, together with improved child health, rather than the uncontrollable factors of cyclic virulence of the virus and of inherited immunity, which has caused the diminution in the death rate is supported to some extent by the change in the types of complications. Involvement of the respiratory tract, otitis media and mastoiditis are less frequent, and noma has become extremely rare. Activation of tuberculosis is less frequently observed, because of the lessened incidence of tuberculous infections; but the incidence of encephalitis, due presumably to the virus of measles itself rather than to a secondary invader, has apparently not been affected.

Attempts to isolate and cultivate the virus of measles have been largely unsuccessful, and dependable prophylactic or therapeutic procedures based on studies of specific etiologic agents have not been forthcoming. Experimental inoculation of human beings may be performed with success and once was used rather extensively.[1] Surprisingly small amounts of blood from patients ill with measles will on subcutaneous injection into normal children induce measles.[2] I have observed that the disease induced by inoculation differs in no way from the natural disease and does not individually run a lighter course. The attempts of Herrman[3] to produce active immunity in infants under five months of age, while they still enjoyed immunity derived passively from the mother, by inoculating them intranasally with secretions from patients acutely ill with measles, represented an interesting step but one which has not been deemed practicable or even entirely safe. When the virus of measles can be successfully cultivated or can even be preserved for long periods to insure its freedom from other organisms or viruses, a trial of the inoculation of patients and subsequent partial immunization with human serum would appear to be justified.

Pending the development of better methods of control, passive immunization with human immune bodies of children after they have been exposed to measles would appear to present the most useful procedure in

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From the Department of Pediatrics, Harvard University Medical School, the Department of Communicable Diseases, Harvard School of Public Health, and the Infants' and Children's hospitals.

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the prevention or modification of the disease. Yet with complications occurring less frequently, because of better understanding of the dangers of measles, and with the death rate steadily declining, even this procedure need not be used indiscriminately.

Antibodies against measles are found in the blood of almost all patients who have recovered from the disease. The titer of these antibodies is greater in patients recently convalescent but in most persons apparently persists in protective quantities throughout life; possibly, it may be augmented somewhat by repeated exposure to patients with the active disease. The utilization of convalescent serum tried by Weisbecker,[4] Cenci [5] and others owes the impetus to its wide use to the reports of Nicolle and Conseil,[6] Richardson and Connor [7] and Degkwitz.[8]

Numerous confirmatory studies have established that serum taken from patients recently recovered from measles, administered by intramuscular injections in doses of 4 or 5 cc. to nonimmune exposed persons in the first few days following exposure, results in a temporary immunity in the recipient, preventing the development of measles from this exposure. If the serum is given late in the incubation period, the temporary immunity is inadequate to insure complete protection and a modified form of the disease ensues. In the modified type, the incubation period is often prolonged; this necessitates lengthening the quarantine period for children who have received the serum. The severity of the disease is reduced, the complications and sequelae are minimized and the attenuated attack usually results in permanent immunity. From the standpoint of public health, the desirable use of serum, especially in the case of normal healthy children who have been exposed, would be thus to induce modification of the disease. However, the degree of modification which can be effected and still permit the development of permanent immunity has not been defined. Debré [9] has maintained that all the symptoms, though in a mild form, must appear if lasting immunity is to result.

When measles breaks out in an institution, hospital, school or convalescent home, modification would not appear to be desirable; rather, the immediate and complete eradication of the disease should be sought, since the attenuated form is still readily communicable and does not eliminate the necessary periods of quarantine. Furthermore, in hospitals many of the patients fall into the groups of acutely or chronically ill, debilitated, or very young children, for whom the fatality rate for measles is highest and who should therefore be protected if possible.

Certain hospitals have for a number of years used convalescent serum effectively in the control of measles. However, even in hospitals the use of convalescent serum has been limited by the lack of adequate supply; control of measles by this means in the general population would be entirely impracticable.

Adult immune serum and adult whole blood have been used as substitutes for convalescent serum [10] on the basis that adults who have experienced the disease retain antibodies capable of protecting other persons. The dose of adult serum must be much larger than that of convalescent serum (15 cc. of adult serum or 30 cc. of adult whole blood, as opposed to 4 or 5 cc. of convalescent serum). The results are less certain than when convalescent serum is used.

The results with the use of adult serum have led to the general acceptance of the observation that the blood (and possibly the tissues) of most urban adults contains the protective antibodies. Furthermore, if the mothers are immune, infants during the early months of their lives are also immune to measles, apparently by reason of the passage of antibodies from mother to fetus through the placenta. In addition to measles, the new-born infant is usually immune to poliomyelitis, scarlet fever, diphtheria and certain other diseases. The actual presence in the umbilical cord blood of the immune bodies to these diseases has been amply demonstrated.[11] These observations have formed the background of the investigations into the use of the human placenta and the blood contained in it as a source of antibodies against measles.

TABLE 1.—*Incidence of Measles in Massachusetts, 1920-1936*

Year	Case Rate	Death Rate
1920	828.3	9.1
1921	453.0	4.5
1922	583.5	5.5
1923	663.6	7.9
1924	546.6	4.0
1925	693.0	8.1
1926	719.8	8.8
1927	322.0	2.1
1928	985.5	6.3
1929	352.5	2.9
1930	637.8	3.2
1931	387.8	1.5
1932	459.9	1.5
1933	348.9	0.6
1934	1,032.8	2.1
1935	283.2	0.8
1936	641.4	0.8

It has been demonstrated that placental extract can be prepared on a large scale, furnishing an extensive source of measles serum in the form of human immune globulin for use in the prevention or modification of the disease.[12]

A comparison of the efficacy of adult serum, convalescent serum and placental extract in the prevention and modification of measles is shown in table 2. The figures are on exposures both in institutions and at home, so are not as rigid a test of the materials as

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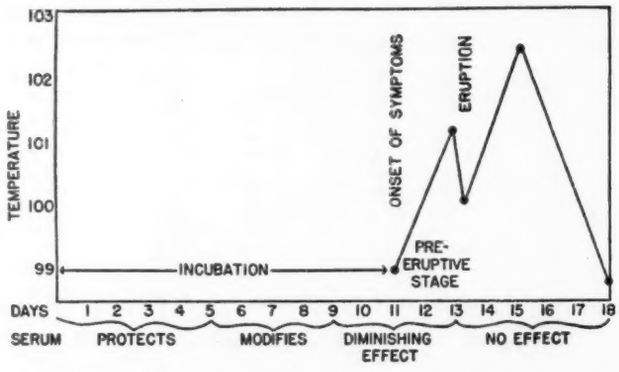
would be figures on a series of persons all known to have been intimately exposed to the disease. They do indicate that fewer failures are to be expected from the use of convalescent serum or placental extract than from the use of adult blood.

The dosage of placental extract as well as that of convalescent serum or adult blood may be influenced by several factors, notably potency, time of administration, age and size of patient and possibly degree of exposure. The only direct method of determining the potency of placental extract has proved to be to test each lot for its ability to prevent measles. The indirect method of using diphtheria antitoxin content as a measure of measles antibodies has been unsatisfactory because the diphtheria antitoxin is apparently segregated almost entirely in the pseudoglobulin fraction of the extract whereas the measles antibody is more generally distributed among the globulins. To base the dose on the nitrogen content of the extract has been a relatively satisfactory method of adjusting dose to potency.

The time of the administration of the antibody is undoubtedly important in determining whether prevention or modification will ensue. Larger doses of immune



Effect of convalescent serum or placental extract on the usual course of measles.

globulin or convalescent serum may offset to some extent late administration, but after the appearance of the rash no effect of the antibodies has been observed. Another factor is the age and the weight of the patient, for, in general, larger children have required larger doses of serum to insure reasonably effective passive immunization. It is well established that infection occurs much less frequently in children exposed in institutions than in those exposed to a brother or sister in the home. The economic status of the home is also important, as exposure in crowded homes is especially intimate and therefore more likely to give rise to infection.

In the accompanying chart is indicated the proportion of the incubation period in which protection or modification of the disease may be expected to follow the injection of either convalescent serum or immune globulin. If serum is given in adequate amount during the first five days of the incubation period the child does not usually acquire the disease. If, however, the injection of serum is delayed from the fifth to the eighth or ninth day, modification is more likely to follow. After the ninth day the serum may have little effect, although with larger doses some influence has been observed even through the preeruptive stage of the illness. After the eruption appears, no effect has been demonstrated from the injection of serum or extract.

In table 3 is shown a more detailed analysis of the results obtained in a study conducted jointly by the Department of Pediatrics, Harvard University Medical School, and the Massachusetts Department of Public Health on the use of immune globulin derived from the placenta in the prevention and modification of measles. The figures for patients intimately exposed are particularly noteworthy, as they represent a rigid test of the efficacy of the material. The separation of the cases into groups according to the effect sought is less accurate, because the beginning of exposure often could not be definitely established. The administration of the placental extract to produce modification of the disease has presented a somewhat difficult problem in the adjustment of doses and the time of administration. Many children received extract either too early or in too large amounts and were completely protected, whereas in a few cases the extract was administered in inadequate amounts or too late, with failure to secure definite modification. Recently, dependable results have been obtained in securing modification by giving extract on the eighth day after exposure in doses ordinarily effective for prevention when given at an earlier date.

Of all children who received the extract without regard for the type of exposure, the proportion protected entirely was 64.3 per cent; a further 30.4 per cent showed modification, and 5.3 per cent showed failure of the extract to produce either protection or modification.

TABLE 2.—*Comparison of the Efficacy of Adult Serum, Convalescent Serum and Placental Extract in the Prevention and Modification of Measles (All Types of Exposures), Based on Figures Collected from the Literature*

Source of Immune Bodies	Number of Cases	Protected		Modified		Failed	
		Number	Per Cent	Number	Per Cent	Number	Per Cent
Adult serum	584	329	56.4	139	23.8	116	19.8
Convalescent serum	1,627	1,227	75.4	273	16.8	127	7.8
Placental extract	2,740	1,762	64.3	833	30.4	145	5.3

TABLE 3.—*Placental Extract in the Prevention or Modification of Measles (Intimate Exposures)*

	Given to Protect				Given to Modify			
	Cases	Protected	Modified	Failed	Cases	Protected	Modified	Failed
Laboratory extract	556	302	222	32	1,159	512	556	91
Commercial extract	29	13	13	3	104	70	30	4
Total	585	315	235	35	1,263	582	586	95
Percentage		53.8	40.4	5.8		46.1	46.4	7.5
		94.2				92.5		

The extract in liquid form has retained its potency for upward of a year. Since the work of Flosdorf and Mudd and of Stokes,[13] the lyophile process of preservation has been applied to some lots of the extract.

The administration of placental extract intramuscularly has been followed in some instances by local or

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general reactions. Somewhat more than 57 per cent of the children had no reaction of either type after the injection of the extract (table 4); 36 per cent had a local reaction of sufficient degree to be called to the attention of the attending physician, but only 5 per cent suffered a local reaction great enough to be classed as moderately severe; a febrile reaction occurred in 19 per cent of the patients, and in 3 per cent the temperature rose above 101 F. Since some children had both local and febrile reactions it seems safe to say that in about 8 per cent of cases there were reactions that could be considered moderately severe.

Immediate and late allergic reactions to serum presumably should not occur with a protein of human origin. Nevertheless, three cases of accelerated serum disease are known to have occurred in the total number of patients receiving placental extract. One similar reaction was observed after the injection of convalescent serum. Two of the reactions to placental extract occurred in children known to be allergic; the third child had no previous allergic history.

Injections of convalescent serum or of placental immune globulin have not been found to sensitize to subsequent injections of the material. A number of patients received two or more injections at intervals

TABLE 4.—*Placental Extract; Reactions to Intramuscular Injection*

Total Number of Cases	No Reactions		Local Reactions: Mild		Local Reactions: Moderately Severe		Febrile Reactions: Mild		Febrile Reactions: 101 F. or Over	
	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
2,896	1,659	57.2	1,058	36.7	142	4.9	578	19.9	86	2.9

varying from a few weeks to several months, yet in no instance were the second or subsequent injections followed by local reactions of more severity than were observed after the first injection, and in no instance were there any manifestations of specific sensitization.

Immunity following the injection of either placental extract or convalescent serum is passive and therefore of short duration. Observations on fifty-four children reexposed to measles within a few weeks after receiving immune globulin indicate that the immunity resulting from the injection was insufficient to protect against reexposure occurring more than two weeks after the administration of the protective dose and that seldom did even modification occur if reexposure took place more than three or four weeks after the injection.

SUMMARY

Despite the inadequacy of the public health control of measles and the lack of a means of active immunization, there has been a steady decline in the death rate for the disease. This decline is thought to be due to recognition of the dangers of measles, prevention of needless exposure of young children, isolation of patients with measles from one another to prevent cross-infection with secondary organisms and a general improvement in child health and nutrition.

Human immune bodies in the form of convalescent serum, adult immune serum or placental extract may be used to prevent or to attenuate the disease. Immune globulin, human (placental extract), as a source of material, and the lyophile process of preservation have made human immune bodies more widely available. If serum is to be used at all in normal healthy children, it should be given sufficiently late in the incubation period, i. e., between five and nine days after exposure, so that attenuation of the disease is obtained, as permanent immunity usually follows. Complete protection by the use of human immune bodies is of short duration, lasting only a few weeks, and is of particular advantage when used in institutions or for acutely or chronically ill, debilitated or very young children.

ABSTRACT OF DISCUSSION

DR. SAMUEL KARELITZ, New York: I have treated more than 200 children prophylactically for measles with the whole globulin preparations of the placenta and have worked out a method for determining the correct dosage. My results indicate that immune placental globulin is effective if the dosage is properly considered, but the reactions to the injections were too severe to continue their use. The earlier commercial placental products gave poor results, because there was no way of knowing what amount of effective substance was injected. I have tested the more recent refined and concentrated preparations of immune globulin (human) in about sixty-five children. Of these, forty-two were carefully observed. I obtained only 62 per cent beneficial results. I failed to get modification or protection in 38 per cent of the cases. Failure was encountered in 25 per cent of the children injected with as much as from 3.5 to 8 cc. Fourteen children injected with from 4 to 10 cc. of immune globulin (human) therapeutically in the preeruptive stage of measles failed to show improvement. They seemed worse because of the severe reactions to the injections. This is in striking contrast to some of the reported results. I believe that the placental globulin preparations are effective in measles prophylaxis, but the results are too inconsistent as yet, especially when complete protection is sought. Therapeutically, it is entirely disappointing in the dosage recommended. My earlier studies with placental globulin led to the opinion that the source of the placental antibodies was the maternal circulation. Since the placental antibodies originate in the maternal circulation, and since the blood of gravid women is no more effective than other immune adult blood, and since blood is much easier than is placenta to work with, I prepared globulin extracts of pooled immune adult blood serum. The results with the first preparation reported on in 1934 indicated that good results could be obtained and that the idea of using pooled immune adult blood was feasible. A month ago I reported before the Society for Pediatric Research my results obtained with two concentrated globulin preparations made from pooled immune adult blood serum. Seventy-three children intimately exposed to measles in their homes were innoculated with from 1.5 to 7.5 cc. of these preparations. In 98 per cent, or all but one child, either no measles or definitely modified measles resulted. Only one child had manifest complications. Neither a local nor a general reaction was observed in any case. The small volume needed, the absence of reactions, the relative ease of preparation, the almost universal availability of immune adult blood, the simplicity of determining the dosage, the ability to store and transport the product and, above all, the good results obtained in measles prophylaxis, with the globulins of immune adult serum, are adequate reasons for recommending its use in the prophylaxis of measles.

DR. CLIFFORD D. SWEET, Oakland, Calif.: My experience indicates that measles may generally be prevented if one gets a good convalescent serum and gives it to the child immediately after exposure. When a child is in such a state of health, that measles would be dangerous, immune serum should be injected at once. About five years ago I rather enthusiastically injected adult human immune serum for the purpose of modifying measles, injecting it about four days, on the average, after known intimate exposure, and obtained a very large number of children who had modified measles, ranging from measles

which had all the symptoms but which did not make the child very ill, to some that were scarcely recognizable, having perhaps Koplik spots and a scattering but definite rash. I reported those cases in *California and Western Medicine* by request at that time. This year, during another outbreak of measles, I had about ten patients with severe recurrent measles in private practice, all of whom had previously had modified measles. Three or four of these children who had their second attack of measles this year had as severe measles as I have seen in the community, having in mind that in the various epidemics of measles which I have observed there has been considerable variation in the severity during different seasons.

DR. HAVEN EMERSON, New York: I should like to ask Dr. McKhann whether he has considered the possible error in attributing a drop in the case fatality rate to changes in treatment. I think health officers would be inclined to say that the main factor in the drop in case fatality has been the increase in the reporting of measles, which is commonly a large factor in dropping case fatality rates of reportable disease. There is one other factor that I think should be taken into consideration, and that is the rapid and considerable drop in the birth rate, which has been probably the most important factor in the cutting down of the measles mortality in the United States. The dropping of the birth rate has diminished the number of persons in the population subject to the mortality of measles. I doubt whether there is evidence justifying the claim for the practitioner of medicine, or for any therapeutic procedures, of responsibility for the reported lower case fatality percentages.

DR. FRANKLIN P. GENGENBACH, Denver: I have used convalescent measles serum for more than ten years with very good results. I have given from 5 to 10 cc. intramuscularly within a few days of definite exposure to induce a modified attack and from 10 to 20 cc. immediately after exposure to prevent an attack. In Denver, as in other large cities, we are fortunate in having proper hospital and laboratory facilities for obtaining and preparing convalescent serums. I can see that the commercial placental extract might be of considerable value in smaller communities.

DR. CHARLES F. MCKHANN, Boston: Most of the points that have been brought up in the discussion were covered in the original presentation, with the exception of Dr. Emerson's. We have in the state of Massachusetts from 13,000 to 40,000 cases of measles every year, the increases recurring in cycles of from three to four years. The death rate from measles has gone steadily down; if this were due to better reporting, the case incidence should have gone up. This has not taken place, because the incidence remains essentially the same as it has been over the last sixteen or eighteen years, but the death rate has gone steadily down throughout that period. I did see the bulletin of the American Public Health Association but still hold the view that there are actually fewer deaths from measles rather than an apparent diminution. We make no claims that it is therapy which has reduced the deaths from measles. I think I stressed very strongly that there is a general improvement in child health throughout the country, which has been an important item in the drop of the fatality rate. We no longer see the same number of children who are tuberculous, debilitated or suffering from deficiencies. I don't think clinicians have claimed or even think they should claim the credit for the reduction in communicable diseases. They think it should be shared with our public health friends. As far as the lower birth rate having an effect on the death rate of measles, that is the same thing I was talking about; namely, keeping very young children out of contact with the disease.

The Natural End of All Cults.—There is nothing homeopathic about the scalpel, and when surgery was permitted to creep into this doctrinaire school it was near its end. The osteopath and chiropractor and eclectic and all the others may beware of this, for so soon as they come to engage in surgery, then a thorough medical grounding will be necessary; hence the natural end of all such cults is that, dead or alive, they will become swallowed in time by the general profession, distasteful as the dose may be.—Cushing, Harvey: Consecratio Medici and Other Papers, Boston, Little, Brown & Co., 1928.

COMPLETE HEART BLOCK ASSOCIATED WITH PNEUMONIA AND PERITONITIS

REVIEW OF THE LITERATURE AND REPORT OF A CASE IN WHICH A LESION WAS DEMONSTRATED HISTOLOGICALLY

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It is generally conceded that, among acute infections, rheumatic fever is the most common cause of heart block. Diphtheria, influenza, scarlet fever, tonsillitis and subacute bacterial endocarditis also have been considered as etiologic agents. There have been very few reports of cases in which heart block occurred during or immediately following pneumonia. The majority of these patients have recovered from the infection and there has been a subsequent disappearance of the arrhythmia. No cases of heart block associated with peritonitis could be found in the available literature.[1]

REVIEW OF THE LITERATURE

In 1912 Dykes [2] reported a case in which a man, aged 23, had typical lobar pneumonia. This patient was not critically ill at any time and on the seventh day the fever fell by crisis. This was followed by a week of uneventful convalescence, at the end of which irregularity of the pulse was noted. A tracing of the jugular vein and carotid artery revealed that the AC interval was prolonged and that there were dropped ventricular beats. Later there appeared a 3:1 heart block. This arrhythmia lasted three weeks and then disappeared. The patient was reexamined three months later and was still normal. Dykes could find no reference in the literature to heart block associated with pneumonia. Cowan and his associates [3] reported a case in which a man, aged 26, died of a subacute bacterial endocarditis. The blood culture was negative but an infarct of the spleen revealed pneumococcus and Escherichia coli. The polygram in this case showed a prolonged AC interval (0.25 second). Serial sections revealed that the auriculoventricular node was normal except for marked congestion. In the bundle of His there were three foci of round cell infiltration, two of which were of moderate size and showed degeneration of the adjacent cells. This case is mentioned because the pneumococcus was found, but it should be emphasized that the conduction time was merely delayed. The lesion of the bundle of His was probably an extension from the bacterial vegetations found on the mitral valve.

Neuhof [4] reported two cases in which heart block occurred in the presence of pneumonia. The first patient was a man, aged 70, who was admitted to the hospital in a semicomatose condition. There was a history of an illness of undetermined nature for several months prior to his admission. Examination revealed marked paralysis agitans and a pulse rate of 36 per

From the Section on Cardiology, the Mayo Clinic.

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3. Cowan, John; Fleming, G. B., and Kennedy, A. M.: Heart Block and Nodal Rhythm in Acute Infections, Lancet **1**: 277-283 (Feb. 3) 1912.
4. Neuhof, Selian: Functional Heart Block in Pneumonia, J. A. M. A. **63**: 577-579 (Aug. 15) 1914.

minute. A polygraphic tracing showed a complete auriculoventricular dissociation. The patient died and necropsy revealed scattered areas of pneumonia. In serial sections there was no lesion of the bundle of His, except a slight increase in fibrous tissue. In the auriculoventricular node there was only slight fatty infiltration. No mention was made of sections through the right and left branches of the bundle of His but such studies are very important, especially when the auriculoventricular node and the bundle of His are entirely or practically normal. Yater, Cornell and Claytor [5] have shown that bilateral lesions of the bundle branches are often the cause of auriculoventricular dissociation. Furthermore, the advanced age of this patient, his illness, which was of several months' duration, and the slight fibrosis of the bundle without acute changes all suggest that the disturbance in conduction might have been the result of arteriosclerosis. Neuhof's second patient was a man, aged 49, who had lobar pneumonia. One ounce (30 cc.) each of tincture of digitalis and digalen was given prior to the onset of the bradycardia, but no vomiting occurred. The temperature dropped by crisis on the fourteenth day and two days later the pulse rate suddenly fell to between 30 and 44 beats a minute. This rate persisted for a week, during which time the patient was in collapse and semistupor. Nevertheless, the pneumonia continued to resolve. No generalized convulsions occurred but periods of muscular twitchings, deep coma and a barely perceptible pulse were observed. These attacks averaged about one minute in duration. The polygrams were unsatisfactory but it seems highly probable that the patient had a complete heart block. A week after the bradycardia began, the patient suddenly showed marked improvement and his pulse rate was found to have returned to normal. The convalescence continued uneventfully except for a few short periods during which the bradycardia returned.

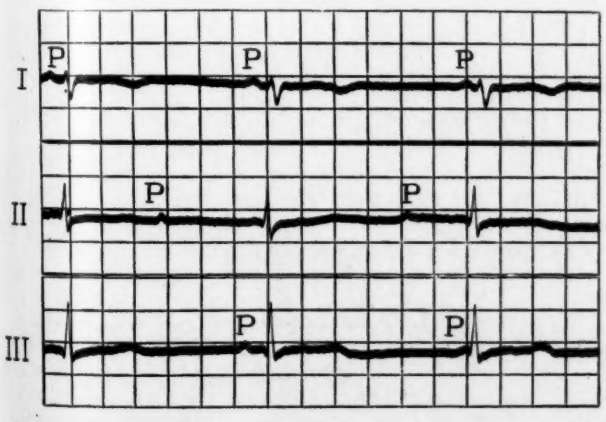

Fig. 1.—Electrocardiogram taken two days after the onset of the bradycardia; there is complete auriculoventricular dissociation; auricular rate 40 and ventricular rate 47.

Frommel and Thévenod [6] reported a case in which there was electrocardiographic evidence of complete auriculoventricular dissociation during pneumonia. The patient was 78 years of age. Following recovery, a two to one block persisted. The authors believed that the block may have been present before the onset of the pneumonia. The age of the patient, the persistence of the defective conduction and the administration of digitalis during the acute illness all make it very likely that the defect in conduction was the result of previous arteriosclerosis. Von Kiss and Wollek [7] reported a case in which a boy, aged 4 years, had lobar pneumonia which involved the entire left lung. The fever terminated by crisis on the seventh day. The pulse rate fell to 76

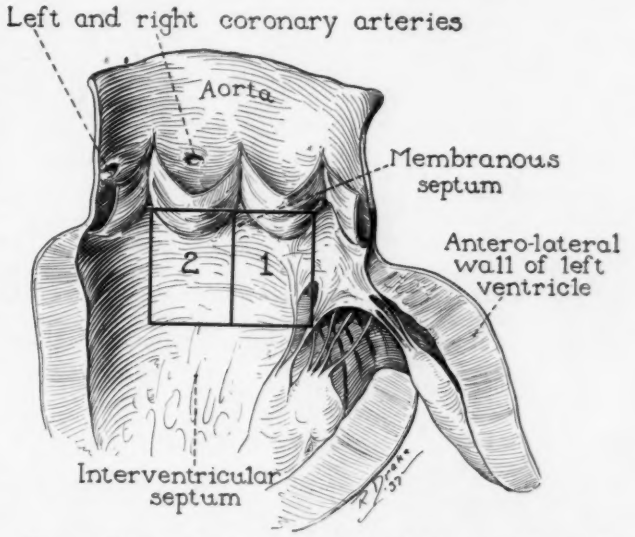

Fig. 2.—Diagram of a heart showing the blocks removed for section; block 1 includes the auriculoventricular node and the first portion of the bundle of His; block 2 contains the remainder of the bundle of His and the proximal parts of its right and left branches.

and finally to 60 beats per minute and was irregular. The electrocardiogram revealed a PR interval of 0.25 second; there also were dropped beats. The child made a rapid recovery and the electrocardiogram returned to normal. When the patient resumed activity, the partial heart block promptly returned. Rest in bed for five weeks caused the arrhythmia to disappear permanently.

Yater, Cornell and Claytor, and Mahaim [8] reviewed the literature on complete heart block with detailed histopathologic studies and found forty-eight acceptable cases. They failed to find a case in which the condition was associated with pneumonia or peritonitis.

It is hoped that the report of the following case may help to arouse interest in disturbances in conduction which are associated with acute infections. Considerable attention has been given to the role of acute rheumatic fever, and many articles have been written on diphtheria and a few on influenza. Other causes have been mentioned only occasionally in the literature.

It is rather amazing that in the forty-eight cases previously referred to, there was not a single case of auriculoventricular dissociation, due to acute rheumatic fever, that had been studied by serial sections and reported in detail. There was, however, one case in which the condition was caused by diphtheria and another in which it was caused by tuberculosis. Gross and Fried [9] studied the bundle of His in sixty cases of rheumatic heart disease, both acute and chronic. Although only one or two sections were examined in each case, 60 per cent showed either exudative or vascular changes. When a marked bradycardia or an irregularity of the pulse occurs in an acute infectious disease, an electrocardiogram is indicated, for it is only

5. Yater, W. M.; Cornell, V. H., and Claytor, Thomas: Auriculoventricular Block Due to Bilateral Bundle-Branch Lesions: Review of Literature and Report of Three Cases with Detailed Histopathological Studies, Arch. Int. Med. **57**: 132-173 (Jan.) 1936.

6. Frommel, E., and Thévenod, A.: Blocage auriculo-ventriculaire complet et transitoire au cours d'une pneumonie, Arch. d. mal. du cœur. **10**: 528-532 (Aug.) 1926.

7. von Kiss, Paul, and Wollek, Bela: Herzblock beim Kinde im Anschluss an eine kroupöse Pneumonie, Arch. f. Kinderh. **104**: 38-41, 1934.

8. Mahaim, I., quoted by Yater, Cornell and Claytor.[5]

9. Gross, Louis, and Fried, B. M.: Lesions in the Auriculoventricular Conduction System Occurring in Rheumatic Fever, Am. J. Path. **12**: 31-44 (Jan.) 1936.

by this means that an arrhythmia may be proved beyond any doubt. When patients who have defective conduction come to necropsy a thorough investigation of the conduction system should be made by serial sections. A better understanding of the pathologic changes may enable physicians to advance further in the prevention and treatment of this serious complication. In the large majority of cases in which recovery from the primary infection occurs there is a disappearance of the heart block; nevertheless, the presence of complete auriculoventricular dissociation, especially when associated with the Stokes-Adams syndrome, may cause a fatal termination in an otherwise nonfatal case.

REPORT OF CASE

A girl, aged 15 years, registered at the clinic March 12, 1937, because of generalized abdominal pain which had been present for two days. March 6, 1937, two days after she had played basket-ball, she had noticed mild soreness across the abdomen; this had persisted one day. March 8 she had had a slight chill and had felt lightheaded. The following day she had left school because of dizziness. These symptoms had persisted and on the day before she came to the clinic she had suffered from generalized abdominal pain accompanied by vomiting. Her past history was negative and her family history did not reveal anything of importance.

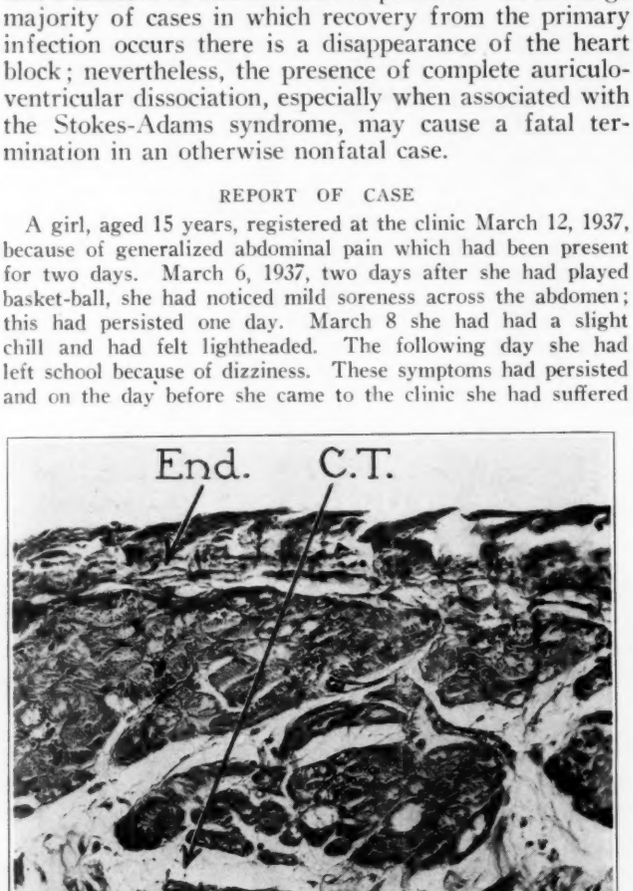

Fig. 3.—The left branch of the bundle of His occupies most of this illustration; the fine stippling seen in the cells is the granular degeneration; a few cells show a hollow center; the endocardium (*End.*) is seen above the bundle and the connective tissue (*C. T.*) below; the underlying myocardium is not shown; specimen stained with hematoxylin and eosin, slightly reduced from a photomicrograph with a magnification of 150 diameters.

The patient was well developed, slightly obese and weighed 136 pounds (61.7 Kg.). The value for the systolic blood pressure was 95 mm. of mercury and that for the diastolic pressure was 80 mm. of mercury. She obviously was acutely ill. The temperature was 103.2 F., the respiratory rate was 24 and the pulse rate was 106 beats per minute. There was a moderate degree of tenderness and rigidity of the entire abdominal wall, but this was most marked in the right lower quadrant. The result of examination of the heart, lungs and other systems was essentially negative.

Analysis of a catheterized specimen of urine revealed a specific gravity of 1.022, an acid reaction, a moderate amount of albumin and an occasional leukocyte. Daily analysis of passed specimens did not reveal any significant variation. The leukocytes numbered 34,700 per cubic millimeter of blood. A differential blood count revealed 22 per cent lymphocytes, 9 per cent monocytes and 69 per cent polymorphonuclear leukocytes; 40 of the last were nonfilamented and 29 were filamented.

The sedimentation rate was 95 mm. in one hour. It was rather apparent that the patient had a generalized peritonitis but the etiology remained obscure. There was no history or other evidence that would cause one to suspect pelvic inflammatory disease of a specific nature, nor was there any history of appendicitis. The prominent signs in the right lower quadrant of the abdomen were the only indications that the appendix was the causative factor. Because of the extensive peritonitis and toxemia, it was decided that conservative measures offered a better prognosis than surgical intervention. The course of the illness was about stationary for four days after her admission; the temperature varied between 101 and 103 F. and the pulse ranged between 100 and 120 beats per minute. March 16, the fifth day of hospitalization, pain developed, and slight dulness and tubular breathing were noted beneath the tip of the right scapula. Roentgenologic examination confirmed the clinical diagnosis of pneumonia, which involved the lower lobe of the right lung. In spite of this complication, her general condition improved slightly. March 18, the third day following the onset of pneumonia and the eighth day of hospitalization, the pulse rate dropped from 104 to 64 beats per minute and remained between 50 and 60 for the duration of illness. The fall in pulse rate developed gradually over a period of twelve hours.

An electrocardiographic tracing, made two days after the onset of bradycardia, revealed a ventricular rate of 47 and an auricular rate of 40 beats per minute, with complete dissociation (fig. 1). Another tracing, made two days later, did not show any significant change.

March 22, the patient was improving. The temperature had not been as high as 101 F. for the past four days and the abdominal pain and tenderness had largely subsided. The pneumonia was resolving satisfactorily but the pulse rate remained about 50 beats per minute. Suddenly, at 9:05 p. m., the patient became dyspneic and cyanotic and died within a few minutes.

Necropsy revealed a generalized peritonitis; about 2 liters of slightly purulent fluid was found in the peritoneal cavity. On the coils of intestine there was abundant evidence of fibrinopurulent exudate and the omentum had migrated to the right lower quadrant of the abdomen. The appendix was normal, while in the fallopian tubes there was a mild secondary salpingitis.

In the right pleural cavity there was about 200 cc. of yellow turbid fluid, and a thick fibrinopurulent exudate was found between the lower lobe of the lung and the pleura. The lung was essentially normal except for evidence of a resolving pneumonia beneath the pleuritis. The left pleural cavity contained about 100 cc. of the same type of yellow turbid fluid, but the pleura and lung were normal.

The heart weighed 304 Gm. and was reddish brown; the usual amount of epicardial fat was present. There was no evidence of fatty change, fibrosis or degeneration in the myocardium. The four chambers of the heart showed neither hypertrophy nor dilatation. The appendages, the endocardium and the valves were normal. The foramen ovale was anatomically open but functionally closed. There was practically no coronary sclerosis. Cardiac measurements were within normal limits.

The exudate covering the peritoneum consisted almost entirely of fibrin and pus cells; there was no evidence of organization. Many gram-positive diplococci were found. It was necessary to embalm the body before necropsy because only a small abdominal incision was authorized. Nevertheless, an attempt was made to take cultures of the peritoneal fluid and exudate in those parts which showed the least evidence of embalming. The cultures failed to reveal any pneumococci or other organisms.

The exudate covering the right lower lobe of the lung exhibited the typical picture of the exudate of an acute pleuritis with early organization. Many gram-positive diplococci were found. The lower lobe of the right lung showed advanced organization and there were many areas of adult connective tissue. These changes in the lung extended for about 3 mm. beneath the pleural exudate. The remainder of this lobe contained a few mononuclear cells within many of the alveoli but was otherwise normal. The remaining lobes of the lungs were normal. Sections of other organs were practically normal.

Several sections of the myocardium taken at various sites in the septum and ventricles were studied and found to be

normal. Sections that were cut after freezing contained no stainable lipoids. Three blocks of tissue were removed for serial sections. One block included the auriculoventricular node and the first portion of the bundle of His and also included about 1 cm. of the membranous septum and about 3 cm. of the interventricular septum (fig. 2). This method required a longer time for fixing than is otherwise necessary and the sections were so large that only after the shrinkage due to fixation could two of them be mounted on a slide. It was necessary that the long axis of the sections be parallel with the long axis of the slide. This technic reduced the tremendous labor required for serial sections of the conduction system. The second block contained the terminal portion of the bundle of His and most of the right and left branches. It was not necessary to study the more distal branches in this case, because of the nature and extent of the lesion found. The third block included the upper part of the sulcus terminalis and contained the sino-auricular node. This block was sectioned parallel to the sino-auricular node, while the other blocks were cut in a transverse direction to Tawara's node and the bundle of His. All blocks were fixed and were embedded in paraffin, and sections were cut 10 microns thick. In blocks 1 and 2, sections 1 and 2 were mounted on slide 1; sections 31 and 32 were mounted on slide 2, and so on. These were stained with hematoxylin and eosin, except for each fifth slide, which was stained with Van Gieson's stain. It should be emphasized however that, in hearts suspected of undergoing fibrosis, every other slide or every slide should be stained with Van Gieson's stain or some other connective tissue stain. Each twentieth and twenty-first section of block 3 was mounted and stained with hematoxylin and eosin, except for each third slide, which was stained with Van Gieson's stain.

The sino-auricular node appeared normal. The usual central artery was seen but neither this artery nor the arterioles were thickened. No changes were observed in the interlacing muscle and connective tissue cells or in the nerves of the node.

The branch of the right coronary artery which passes from the posterior interventricular septum to supply the node appeared normal. Muscle fibers of the auricle connected with the node in the usual fashion.

The auricular muscle, near the node, showed a slight to moderate degree of granular degeneration with an apparent edema of the cytoplasm. The nuclei appeared normal. The auriculoventricular node was in its usual position on the right of the membranous septum. The size, shape, number of specialized muscle fibers and their whorl-like arrangements were all normal. The arteries and arterioles showed no abnormalities. The cells of the node, however, exhibited the same type of change which affected the nearby auricular muscle. The granular degeneration, apparent edema and pale staining character of the cells was only slight in the node but became more pronounced as the conduction system was traced toward its termination. After the node merged into the bundle of His, the bundle followed its typical course by passing through the membranous septum obliquely and then coming to lie above and to the left of that part of the interventricular septum which joins the membranous septum. In the latter position the left branch began coming off. The bundle revealed the changes already described, but to a moderate degree; as the left branch passed down beneath the endocardium on the left surface of the interventricular septum, the degeneration became more marked. Instead of the normal deep red color, the cells were pale pink and were distended by what appeared to be fluid in the cytoplasm (fig. 3). Granules within the cytoplasm were marked and no striations could be found. No exudative changes were seen. In the left branch these changes were found in all sections. In addition, the myocardium, beneath the bundle of His, exhibited these abnormalities in a small portion, which was 2 mm. long and which extended about 1 mm. beneath the bundle.

The right branch followed its normal anatomic course but it showed even more degeneration than the left branch (fig. 4). It was also similar to the left branch in that the lesion was more prominent in the terminal portion. Brown's-Gram stains revealed no bacteria in any portion of the conduction system.

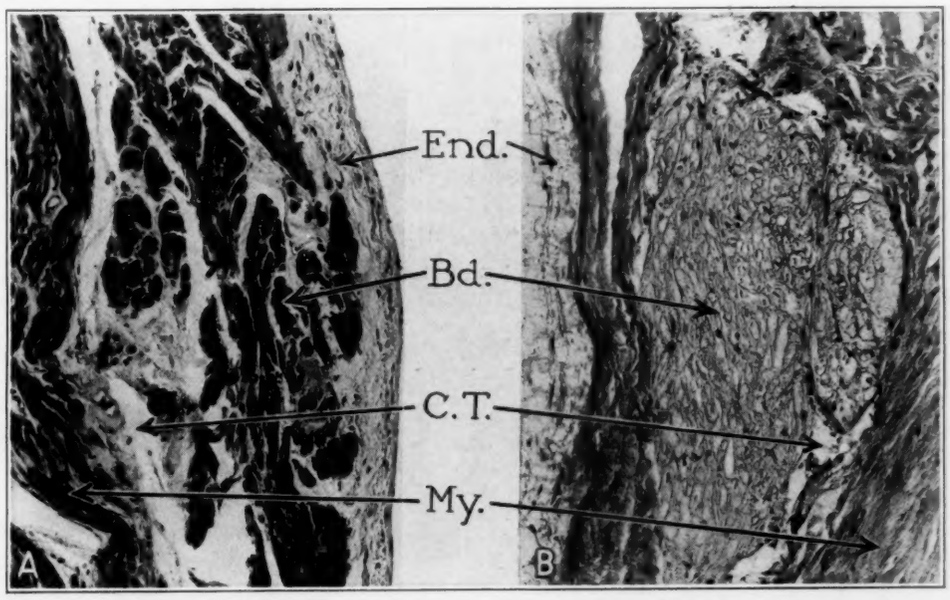

Fig. 4.—*A*, normal right branch of bundle of His; one may note the normal staining reaction and cellular structure; the bundle (*Bd.*) lies beneath the endocardium (*End.*) and is separated from the myocardium (*My.*) by connective tissue (*C. T.*); *B*, the degenerated right branch with its pale-staining reaction; the clear cells are apparently edematous; specimens stained with hematoxylin and eosin; slightly reduced from a photomicrograph with a magnification of 150 diameters.

COMMENT

The moderate degree of acute degeneration found in the auriculoventricular node and in the anterior portion of the bundle of His may or may not have produced the complete auriculoventricular dissociation. However, the changes found in the right and left branches were so marked that if the auricular impulses had been able to reach as far as these branches, they almost surely could have traveled no farther. The finding of similar areas of degeneration in the auricles and ventricle suggest that the conduction system was involved by an extension of this lesion.

Had the peritonitis and empyema subsided, the heart block would, in all likelihood, have disappeared. This is borne out by previous cases of pneumonia and other acute infections. The cellular structure of the conduction system, although degenerated, showed no actual necrosis and probably would have returned to normal.

Signs of peritonitis appeared five days before any evidence of empyema or pneumonia was manifest. However, there was no organization of the peritoneal exudate, whereas that of the pleura was undergoing early organization and the underlying portion of the lung contained young as well as adult connective tissue. It should be recalled that the patient had a chill three days before the onset of abdominal pain.

These observations indicate that the empyema and pneumonia probably preceded the peritonitis but did not become clinically manifest until later.

The gram-positive diplococci found both in the peritonitis and in the pleuritis were probably pneumococci, although this cannot be proved.

There is no clear explanation for the auricular rate of 40. The sino-auricular node was histologically normal. The theory of toxic suppression might be advanced. However, in other cases in which complete heart block is associated with acute infections, the auricular rates are usually normal or rapid.

SUMMARY

In this case a complete heart block developed during the course of peritonitis, pleuritis and pneumonia. The patient died suddenly while recovering from the infection. Necropsy revealed a marked acute peritonitis, acute pleuritis of the right lower lobe and a minimal amount of residual pneumonia. The lesions of the lung and pleura were definitely older than those of the peritoneum. A gram-positive diplococcus was identified in the pleural and peritoneal exudates but cultures were negative. In serial sections of the conduction system there were slight changes in the auriculoventricular node, which became more pronounced as the conduction system was followed toward its terminal portions. These changes were in the form of apparent edema and swelling of the cytoplasm and there also was granular degeneration. There was loss of the striations and the cells which were stained paler than normal. The right and left branches of the bundle of His were affected to a marked degree and in some areas the auricular and ventricular muscle exhibited the same type of degeneration.

FURTHER STUDIES WITH THE TUBERCULIN OINTMENT PATCH TEST

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AND
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SAN FRANCISCO

In previous communications [1] reference was made to the value of the ointment patch test in the diagnosis of tuberculosis. It was shown that the ease of application, the stability of the preparation and the high percentage of agreement with the Mantoux test (0.1 mg. of old tuberculin) made this method a most desirable one for general practice. These previous reports deal with a total of some 800 observations. In the present paper we enlarge on our previous results and report our experience with approximately 1,000 new patients.

HISTORICAL REVIEW

In 1907 Moro [2] first described an inunction method for the diagnosis of tuberculosis. This ointment consisted of 50 per cent old tuberculin in a base of hydrous wool fat. This, however, proved too insensitive for general use. Nevertheless it stimulated many attempts to improve on the percutaneous method. Hamburger [3] introduced the so-called perkutan ointment, which consisted of old tuberculin evaporated to a constant weight. Then followed Moro's diagnostic tuberculin ointment,[4] which was made from evaporated tuberculin of selected cultures, both human and bovine, in a base of hydrous wool fat. Shortly thereafter Löwenstein [5] prepared "dermotubin" from glycerin broth cultures of human tubercle bacilli evaporated to one twenty-fifth volume, filtered and mixed with dead human bacilli equivalent to one-fourth its weight. Moro developed a concentrated tuberculin ointment containing dead tubercle bacilli and keratolytic substances, which is known as ektebin.[6] All the previously mentioned preparations were applied with friction and no adequate control ointment was used. However, Malmberg and Fromm [7] in 1931 devised a tuberculin plaster containing 1 drop of tuberculin per square centimeter and used a control ointment for the first time.

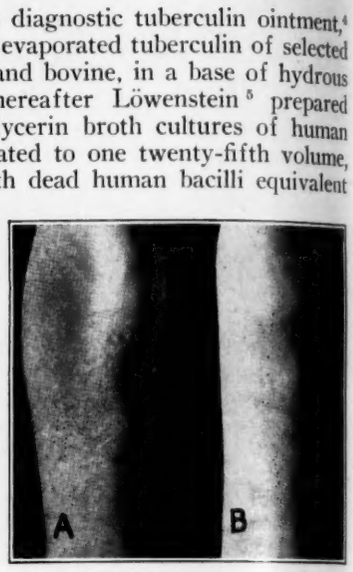

Fig. 1.—Slight positive reaction: (a) ointment patch test and (b) Mantoux test 1: 1,000.

In reviewing the literature on the percutaneous method of tuberculin testing, one is impressed by the fact that comparison in most instances has been made with the Pirquet reaction. The latter method is generally agreed to be definitely inferior to the Mantoux test [8] and has been replaced by it, in America at least. Thus to evaluate adequately any new preparation it should be compared to the most sensitive method at present available for the detection of tuberculous infection, which is the Mantoux test. This we propose to do in the ensuing discussion.

PREPARATION OF THE TUBERCULIN OINTMENT [9]

The ointment employed in this and previous studies was prepared in the following manner: Regular tuberculin glycerin broth was inoculated with human culture H-37. The cultures were incubated for four weeks and then sterilized in the Arnold sterilizer. After sterilization the material was evaporated to one fifteenth of its original volume, the organisms being left in the material. The evaporated and concentrated material was then triturated to a smooth mixture, to which 0.4 per cent phenol was added as preservative. After trituration the material was filled into appropriate tubes. The control material was prepared in exactly the same manner with the exception that the flasks of glycerin broth were not planted with any organisms. The control consisted of the same lot number of broth, and incubation and evaporation were carried out simultaneously with the cultured material.

From the pediatric departments of the University of California Medical School, and of Mount Zion Hospital.

1. Wolff, Ernst: A Tape Test with Tuberculin Ointment, Am. Rev. Tuberc. **27**: 308 (March) 1933; Tuberculin Ointment Patch Test, Am. J. Dis. Child. **47**: 764 (April) 1934.

2. Moro, E., and Doganoff, A.: Zur Pathogenese gewisser Integumentveränderungen bei Skrofulose, Wien. klin. Wchnschr. **20**: 933, 1907.

3. Hamburger, F., and Stradner, F.: Eine Verbesserung der perkutanen Tuberkulinreaktion (Moro), München. med Wchnschr. **66**: 439, 1919.

4. Moro, E.: Ueber ein "diagnostisches Tuberkulin," München. med. Wchnschr. **67**: 1253 (Oct. 29) 1920.

5. Löwenstein, E.: Die Anwendung des Tuberkulins beim Menschen, Handbuch der pathogenen Mikroorganismen **5**: 949, 1928. Maendl, H.: Zur diagnostischen Verwendbarkeit der Loewensteinschen Tuberkulin Salbe, Wien. klin. Wchnschr. **37**: 313 (March 27) 1924.

6. Melion, F.: Der Diagnostische Wert der Applikation von Tuberkulinsalbenpräparaten (Ektebin und Dermotubin), Wien. klin. Wchnschr. **37**: 764 (July 31) 1924.

7. Malmberg, N., and Fromm, B.: Die Tuberkulinpflasterprobe: Eine vereinfachte Methode zur Ausführung der perkutanen Tuberkulinprobe, Acta pediat. **10**: 433, 1931.

8. Reiss, O.: The Mantoux Reaction in Children, Arch. Pediat. **35**: 714 (Dec.) 1918. Greengard, Joseph, and Nichamin, S. J.: The Diagnostic Tuberculin Reaction, J. Pediat. **4**: 393 (March) 1934.

9. Eli Lilly & Co. prepared the ointment at our suggestion and now make it available for clinical trial.

TECHNIC OF THE TEST

The area usually selected for application of the ointment is the inner surface of the upper arm or the paravertebral region between the eighth and the eleventh thoracic vertebra. The skin is cleansed with benzine or ether and dried. A pea-sized drop of the tuberculin ointment is applied on the right side and a similar sized drop of the control material is placed on the left side. Each of these drops is covered tightly with a 1½ inch square of ordinary adhesive plaster, which is removed in forty-eight hours.

Correlation Between Ointment and Mantoux Tests in Different Clinical Groups*

Classification	Number of Cases	Agreement, per Cent	Disagreement, per Cent
Negative Mantoux and x-ray	573	99.3	0.7
Positive Mantoux, negative x-ray	146	93.8	6.2
Positive Mantoux, positive x-ray (clinically latent)	215	97.7	2.3
Positive Mantoux, positive x-ray (clinically active)	141	100.0	0.0
Total	1,075	98.2	1.8

* The Mantoux test was done with 0.1 mg. of old tuberculin. Agreement between the ointment and the Mantoux reaction occurred in 1,056 out of 1,075 instances, or 98.2 per cent. Discrepancies occurred in nineteen cases, or 1.8 per cent:

1. Positive Mantoux 0.1 mg., negative ointment. This disagreement occurred fourteen times, or in 1.3 per cent of total tests. In none of these was there x-ray or clinical evidence of activity.
2. Negative Mantoux 0.1 mg., positive ointment. This disagreement occurred five times, or in 0.5 per cent of total tests.

One of the latter patients showed hilar calcification. In four cases the ointment and the intracutaneous test with 1 mg. of old tuberculin were positive, whereas the injection of 0.1 mg. of old tuberculin had failed to produce a positive reaction. In one of these cases, roentgen examination showed a hilar gland tumor.

Positive reactions are manifested as follows: A weak test shows a few discrete small papules of a pale rose color (fig. 1), a medium reaction consists of many vividly red papules with erythema of the surrounding skin (fig. 2), while a marked positive reaction shows, in addition to the preceding condition, marked induration and yellowish discoloration of the total test area

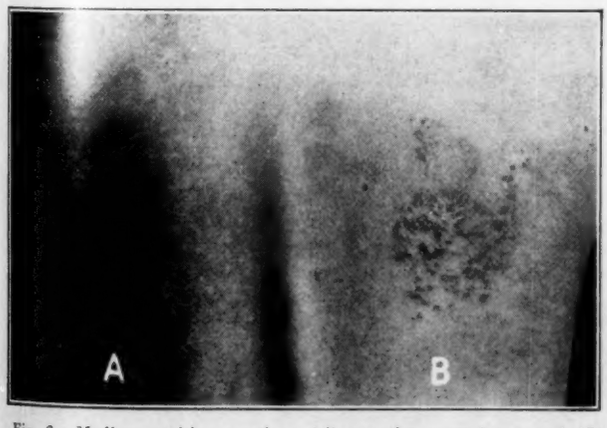

Fig. 2.—Medium positive reaction; (*A*) negative control test and (*B*) ointment patch test.

(fig. 3). Occasionally distinct vesicle formation results. A few papules may rarely be seen under the control tape, but only in strongly positive reactors, and no difficulty in interpretation has been experienced.

The color of the positive reaction area begins to fade in about ninety-six hours but may still be discernible after one week. Scaling and brownish pigmentation of the skin may be seen for several weeks after the marked reaction. In contradistinction to the intracutaneous test there has never been a generalized systemic reaction. The only symptom encountered is itching over the positive test area.

CLINICAL MATERIAL AND RESULTS

This paper is based on a study of 1,075 tests done on 964 patients ranging in age from 3 months to 15

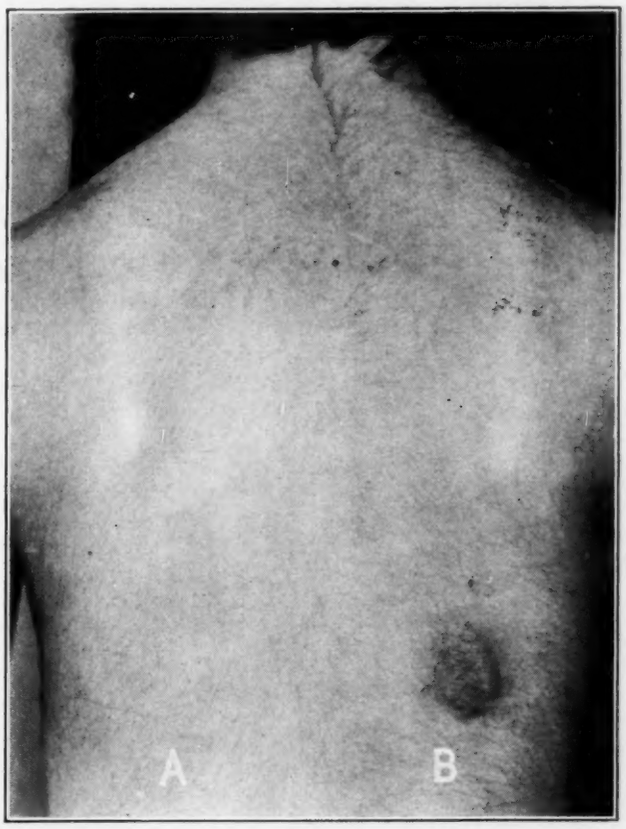

Fig. 3.—Strong positive reaction; (*A*) negative control test and (*B*) ointment patch test.

years. These patients were seen at the children's chest clinic of the University of California Hospital, the outpatient pediatric department of Mount Zion Hospital and the children's tuberculosis wards of the San Francisco County Hospital. These patients were tested simultaneously with the tuberculin ointment and with 0.1 mg. of old tuberculin by the Mantoux method. The accompanying table shows the correlation between the two methods of testing in the different clinical groups.

The high percentage of agreement between the Mantoux and the tuberculin ointment patch test shows the general sensitivity of the latter method. A striking feature is that in no case of a discrepancy in which the ointment method was negative has there been any clinical or roentgenologic evidence of active tuberculous disease. On the other hand, the ointment test has been positive in every instance of active tuberculosis.

COMMENT

Our results with the ointment described have been better than with any other percutaneous application yet employed. Kundratitz[10] in 270 Mantoux (0.1 mg.) positive hospitalized tuberculous children tested with dermotubin found discrepancies in favor of the intradermal method in twenty-three cases, or 8.6 per cent. Somewhat better results were reported by Goldberg

10. Kundratitz, K.: Die perkutane Tuberkulinprobe mittels der Tuberkulin salbe "Dermotubin," Ztschr. f. Tuberk. 42: 222, 1925.

and Gasul,[11] who among 109 children observed only two instances in which the Mantoux reaction proved positive while the dermotubin test was negative. Hille [12] among ninety-six cases positive to 0.1 mg. of old tuberculin intracutaneously observed only eighty-five positive reactors with Moro's diagnostic tuberculin ointment. Although Malmberg and Fromm [7] reported a large series of cases controlled by the Pirquet test, only fifty Mantoux positive reactors were recorded and of these forty-nine proved positive to their tuberculin plaster. Verde,[13] comparing the tuberculin plaster test with the Mantoux reaction (1:5,000), found disagreement in seven cases out of 165 children examined in a routine manner; these discrepancies all favored the intradermal method. In 1935 Anzén [14] reported on a group of 2,183 patients between the ages of 3 days and 15 years and found an agreement between the tuberculin plaster and the Pirquet test in 98 per cent of cases. Among 1,838 patients in whom a negative plaster reaction was found, 806 were further tested by the Mantoux method and 1.25 per cent reacted positively. Among fifty cases found to react positively to our ointment and the Mantoux method, two negative results with the plaster described by Anzén were noted. Furthermore, the tuberculin plaster as at present supplied is messy and rather difficult to work with because it remains closely adherent to the underlying paper to which it is attached. It is also quite expensive for widespread use. Early in this study efforts were made to incorporate purified protein derivative powder into an ointment, but the results obtained were unsatisfactory. As the work progressed further attempts were abandoned because the tuberculin ointment we are employing at present had proved eminently satisfactory over a period of four years' clinical trial.

Fig. 4.—Strong positive reaction with Mantoux test 1:1,000; same patient as in figure 3.

ADVANTAGES OF THE TEST

Given an ointment test which is clinically equivalent to the Mantoux, its advantages are several. The ease and speed of application lend the patch test to general use in private practice and public health work. It overcomes the objection of psychologic shock and pain caused by the use of the hypodermic needle. No false positive reactions are encountered, as a control test is an integral part of the method and the skin area tested is protected as a routine by the adhesive plaster. The ointment is comparatively easy to prepare, is relatively inexpensive and has been found to retain its potency for a period of at least four years.

SUMMARY

1. The agreement between the ointment patch test and the intracutaneous test with 0.1 mg. of old tuberculin in 1,075 observations was 98.2 per cent. This corresponds closely to figures previously reported for some 800 observations. Discrepancies occurred only in clinically latent cases.

2. The ointment test was positive in every case of active tuberculous disease.

CONCLUSION

The results of a tuberculin patch test with control herein and heretofore detailed warrant the conclusion that in our experience the test may safely be substituted for the Mantoux test with 0.1 mg. of old tuberculin in office and public health practice. We feel that it now merits a thorough clinical trial.

450 Sutter Street—University of California Hospital.

11. Goldberg, B., and Gasul, B.: The Dermatubin Test: A Comparison with the von Pirquet, Moro and Mantoux Reactions, Illinois M. J. **58**: 60 (July) 1930.
12. Hille, K.: Zur Technik der perkutanen Tuberkulinreaction nach Moro, Arch. f. Kinderh. **88**: 14 (July 12) 1929.
13. Verde, M.: Sulla prova tubercolinica sotto cerotto adesivo, metodo semplificato della percutaneoreazione, Pediatria **44**: 874 (Oct.) 1936.
14. Anzén, G.: Comparative Values of Cutaneous, Percutaneous and Intracutaneous Tuberculin Tests in Children, Am. J. Dis. Child. **50**: 104 (July) 1935.

MYASTHENIA GRAVIS

REPORT OF A CASE WITH NECROPSY

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AND
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We here report the clinical course of an extremely severe case of myasthenia gravis, the effect of treatment on the disease and the postmortem results. The etiology is unknown and, although there is some agreement as to the primary microscopic changes in the muscle, each author finds multiple variations in the abnormality of the other organs and each seeks a new theory to explain the disease. Our report is unique in that we shall simply state the facts as we observed them and leave the speculation to others.

REPORT OF CASE

History.—A graduate nurse, aged 27, single, referred to one of us (F. E. B.) with a provisional diagnosis of hyperthyroidism, complained chiefly of loss of weight, nervousness and vocal changes, which began approximately six months prior to admission to the hospital. Increasing fatigue was especially apparent when she walked any considerable distance; it was difficult to swallow or talk, and the face felt "stiff." Before the onset of her illness she weighed 180 pounds (82 Kg.). She voluntarily reduced her weight without medication to 148 pounds (67 Kg.). This was maintained until the present illness. During the six months prior to admission she lost 38 pounds (17 Kg.), became extremely nervous and irritable and had an aversion to food. Ten weeks prior to admission she was confined to bed because of the weakness. The speech became thick and very difficult to understand. Food was regurgitated through the nose, and the length of time it took to masticate a meal was progressively increased. She perspired profusely and was intolerant to heat. Such slight exertion as moving in bed caused palpitation.

The past history was unimportant except that these symptoms followed an illness of several weeks, which she diagnosed as the "grip." While training as a nurse she complained of

From the Massachusetts Memorial Hospitals and the Evans Memorial.

hoarseness and had had periods of fatigability, but as the symptoms were not severe she did not mention them. She had an occasional nonproductive cough. The bowels functioned with difficulty. Menstruation began at the age of 13 years and was always regular and painless.

Physical Examination.—The patient was well developed but emaciated and was dyspneic when talking. The voice was hoarse and nasal. The face was flushed and the skin moist. There was marked ptosis of the eyelids; the pupils were dilated and reacted to light and in accommodation. The tongue was slightly coated and dry. The teeth were in good condition. There was decreased excursion of the palate. The face had a masked expression, and it was impossible for the patient to whistle. There was no enlargement of the heart, the rhythm was regular and the rate was 112. The lungs were resonant, with no abnormal breath sounds. The abdomen showed no masses, spasm or tenderness. There was no edema of the ankles. The fingers showed a fine tremor. It was difficult for her to elevate her legs from the bed, and after three attempts it was impossible to do so at all.

X-ray examination of the skull was negative. The chest showed no evidence of substernal thyroid. The heart was small and concave, the left border exhibiting under the fluoroscope the rate of 120 per minute. Examination of the lungs gave negative results. X-ray films of the pharynx and larynx taken with the patient at rest showed deformity of the ventricles with a flattening of the inferior border and concavo-convex superior border. The appearance was practically unchanged during phonation (letter E). Fluoroscopically there were normal deglutitory movements. The oropharynx was not completely obliterated. There was marked limitation of the upward movement of the hyoid bone and larynx. The epiglottis showed incomplete excursion, and barium was retained in the epiglottic vallecula and pyriform sinuses. There was no apparent evidence of tumor or inflammatory processes.

A special examination of the eyes revealed pupils 5 mm. and reaction normal. Extra-ocular actions were normal. The media were clear. The fundi were normal. The fields were normal by confirmation. Vision was unsteady because of the patient's reduced physical condition. Examination of the larynx revealed no neoplasm. Excursion was definitely less than normal.

Laboratory examinations revealed: Basal metabolic rate plus 29 and plus 19; blood pressure 98 systolic and 54 diastolic. The tuberculin and Schick tests gave negative results. Blood cholesterol was 204 mg. Leukocytes numbered 11,050, neutrophils 70 per cent, lymphocytes 10 per cent, endothelials 11 per cent, eosinophils 3 per cent, hemoglobin 80 per cent, and erythrocytes 4,600,000. The blood count did not change materially throughout the hospitalization. Chemical examination of the blood revealed nonprotein nitrogen 35, 40 and 36; blood sugar 100, 95 and 80. Sputum was negative. A complete urinalysis, characteristic of many, showed an alkaline reaction, specific gravity 1.025, total solids 5.8, urea 3.06, albumin slightest possible trace, no sugar, acetone or bile, a rare pus cell, no blood disks; few large epithelials, some phosphatic crystals, no casts. Creatinine nitrogen and creatine nitrogen readings are given in the accompanying table.

Clinical Progress.—The patient was admitted to the hospital in a state of shock due to a long automobile ride. Following intravenous injection of saline solution and complete rest she showed slight improvement. Specific medication was not instituted until the ninth day. At this time ephedrine sulfate was given according to the dosage suggested by Boothby,[1] 8 grains (0.5 Gm.) dissolved in 8 ounces (240 cc.) of saline solution. One drachm (4 cc.) of this solution was given from three to five times daily, the doses being distributed before and after meals. One drachm of this solution equals approximately one-eighth grain of ephedrine. There was a notable improvement for a time, but after a ten day trial it was necessary to suspend this medication because of an increase in the pulse rate, an increase in nervousness and marked insomnia.

Patients with hyperthyroidism often do not tolerate ephedrine well. There is an aggravation of all symptoms, with a good deal of apprehension. It is possible that a patient with myasthenia gravis with an increased metabolic rate will react to the drug in the same manner. During her stay at the hospital one other attempt was made to give ephedrine in a very much smaller dosage, but this brought about the same results. Therefore, this type of treatment was discontinued. The fact that ephedrine is not helpful in all cases and appears to be even harmful in some has been reported by Irwin[2] and Boothby.[3]

Good nursing, careful feeding and intravenous injection of saline solution led to definite improvement. After two days in which no medication was given other than the regimen just mentioned, aminoacetic acid (glycine, or glycocoll) was given a therapeutic test. The aminoacetic acid was administered as a food, and its effect was supplemented by the use of gelatin. It was given in a daily amount of 30 Gm., divided into six doses. Prior to the use of aminoacetic acid the patient was disturbed by a great deal of thick tenacious mucus. This symptom abated almost immediately. Mastication and deglutition showed a decided improvement. The patient became interested in her surroundings and enjoyed visitors, and her pulse rate attained a lower level. There was a decided increase of timbre of the voice and the muscles of the lower extremity responded longer to stimuli. There was no vomiting. Because of the low blood sugar, varying from 100 mg. to 80 mg., several intravenous injections of 10 per cent dextrose were given. The injections caused an aggravation of symptoms and a greater degree of fatigue. This observation has been reported by Boothby.[3]

Creatinine Nitrogen and Creatine Nitrogen Readings

Date	Creatinine Nitrogen	Creatine Nitrogen	Date	Creatinine Nitrogen	Creatine Nitrogen
5/ 5/35	0.88	1.29	5/31/35	0.492	0.485
5/21/35	1.363	1.194	6/ 1/35	0.392	0.306
5/22/35	0.973	0.990	6/ 2/35	0.499	0.401
5/23/35	0.803	0.790	6/ 3/35	0.478	0.359
5/26/35	0.468	0.535	6/ 4/35	0.381	0.338
5/27/35	0.575	0.711	6/ 5/35	0.522	0.406
5/28/35	0.529	0.393	6/ 6/35	0.397	0.426
5/29/35	0.495	0.426	6/ 7/35	0.346	0.454
5/30/35	0.417	0.377	6/ 9/35	0.368	0.358

In the seventh week of her hospital stay the patient was considerably improved. She had passed through two distinct periods of remission and aggravation. She experienced considerable relief from the profuse perspiration that had been so noticeable when she was first admitted to the hospital.

At this time dimethyl-carbaminic ester of m-oxyphenyl-trimethyl-ammonium-methylsulfate (prostigmin) was administered in the doses suggested by Pritchard[4] and Laurent.[5] The first dose was 5 cc. subcutaneously with 1/100 grain (0.00065 Gm.) of atropine. This caused considerable muscular twitching, increased intestinal peristalsis and a decided sensation of weakness. The dose was reduced to 2 cc. with 1/200 grain (0.0003 Gm.) of atropine three times in twenty-four hours. There was a marked improvement following the use of the drug, this improvement lasting approximately five hours following each injection. Laurent and Walther[6] believe that "the action of eserine, and of its analogue prostigmin, in the relief of myasthenic symptoms has not yet received a wholly adequate explanation. The suggestion that eserine acts by delaying the destruction of acetylcholine by choline esterase at the motor nerve ending seems the only workable hypothesis at present.

1. Boothby, W. M.: Myasthenia Gravis: Effect of Treatment with Glycine and Ephedrine, Proc. Staff Meet., Mayo Clin. **9**: 593 (Oct. 3) 1934.

2. Irwin, P. S.: Myasthenia Gravis, with the Report of a Case, Canad. M. A. J. **32**: 405 (April) 1935.

3. Boothby, W. M.: Myasthenia Gravis, Arch. Int. Med. **53**: 39 (Jan.) 1934.

4. Pritchard, E. A.: "Prostigmin" in the Treatment of Myasthenia Gravis, Lancet **1**: 432 (Feb. 23) 1935.

5. Laurent, L. P. E.: Clinical Observations on the Use of Prostigmin in the Treatment of Myasthenia Gravis, Brit. M. J. **1**: 463 (March 9) 1935.

6. Laurent, L. P. E., and Walther, W. W.: The Influence of Large Doses of Potassium Chloride on Myasthenia Gravis, Lancet **1**: 1434 (June 22) 1935.

Any substance known to facilitate the production or the utilization of acetylcholine might therefore be expected to exercise a favorable influence on myasthenia."

The patient had improved at this stage to the extent that she sat in a chair for fifteen minutes and had taken three steps at a time. When she was admitted to the hospital she was unable to take consommés, water or fruit juices without great difficulty and considerable choking. At this time she was eating solid food (potato, meat, fruits), was sleeping well and could carry on short conversations with a fairly strong voice. Her temperature was normal and her pulse rate was in the nineties. She was very bright and alert and seemed quite happy. This improvement continued until the end of the ninth week.

Suddenly her pulse became accelerated and of poor quality; there was evidence of cyanosis. She was immediately placed in an oxygen tent. Her respirations became more and more

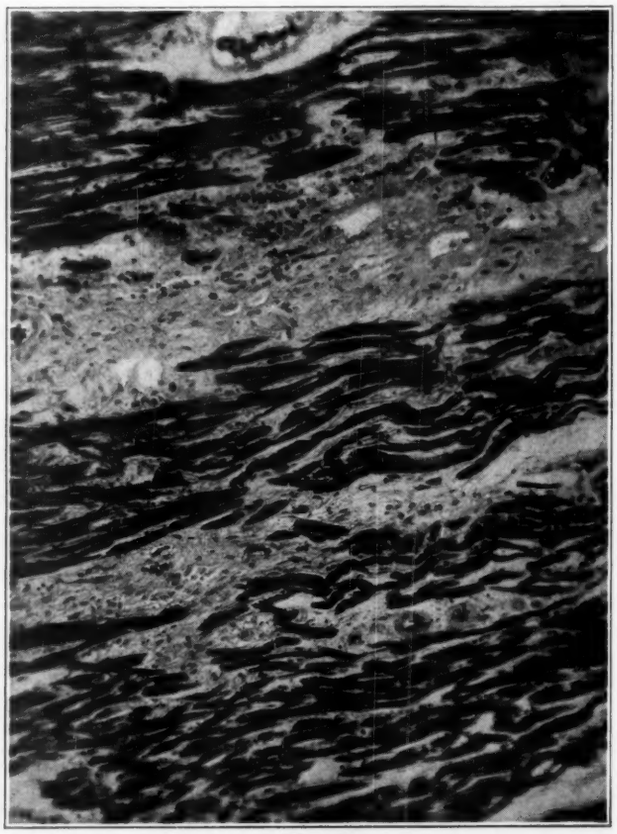

Fig. 1.—Section of the heart showing edema of interstitial tissue, separation of muscle bundles and accumulations of lymphocytes (× 120).

labored, and the cyanosis increased. A tracheotomy was performed and she was returned to the oxygen tent. Prostigmin was given with temporary benefit, but the respirations became more shallow and finally she died of respiratory failure.

COMMENT

The similarity between many of the symptoms of hyperthyroidism and myasthenia gravis, particularly with respect to the syndrome of muscular fatigue, has been discussed by Allen [7] and by Cohen and King.[8]

One of us (F. E. B.) had three similar cases referred with a diagnosis of hyperthyroidism only to have the laboratory and clinical evidence point toward myasthenia gravis. These cases have responded to the usual treatment for this disease.

The basal metabolism in this particular case remained elevated until death, but the thyroid gland failed to show any microscopic changes. Myasthenia gravis should be considered in the differential diagnosis of hyperthyroidism.

Since the changes found at necropsy in myasthenia gravis were first described by Wilks [9] in 1877, numerous authors have published the postmortem examinations in one or more cases, the most comprehensive reports being those of Starr,[10] Bell [11] and Norris.[12] The excellent review of Keschner and Strouse [13] suggests many possibilities.

For some time the disease was thought to be due to changes in the central nervous system. Attention was then shifted to the myoneural junction and a fatigue syndrome. Some have associated it with dermatitis, others with hyperthyroidism. One author made the novel suggestion that the disease was a "perivascularitis chronica proliferans." The seemingly more than accidental association with thymic tumors as discussed by Bell and Norris is disconcerted by those cases in which the thymus is normal or atrophic. The disease has been thought to be due to a toxemia by the majority of writers, though just what the source or type of toxin is has not always been clear. A bacterial theory has been expressed but was never substantiated until Butt [14] found streptococcoid organisms in the tissue from seven cases. Rosenow and Heilman [15] have produced myasthenia-like lesions in animals by injecting toxins from specific strains of streptococci.

Our case resembles many others reported but presents interestingly divergent features. The myocardium showed as marked a myasthenic reaction or "lymphorrhagia" as any of the striated muscle throughout the body. We also noted in all the muscles examined that there were not only evidences of atrophy and Zenker's degeneration of individual bundles but also a distinct inflammatory spectrum. To be sure, this consisted for the most part of the more chronic inflammatory phases with lymphocytic infiltration and fibrosis, as well as the characteristic lymphoid accumulations universally described by others; but other areas were also present in which the edema and neutrophilic infiltration of acute inflammation predominated, albeit the usual capillary engorgement was not pronounced. A consistent lack of any perivascular or specific vascular lesions was noted except in the pancreas. Here one encountered a patchy acute inflammation of the interstitial tissue with relatively little involvement of the parenchyma. The distinct phlebitis and lymphangitis present at one point would be entirely absent in another group of vessels no more than 2 mm. distant.

A severe toxemia was clearly evidenced by the splenitis, the focal necrosis in the liver, adrenals and pancreas, and the mild enteritis. That this was of a peculiar and probably nonbacterial nature is perhaps supported by the fact that the lungs showed very few microscopic changes. Special stains on all the aforementioned tissues and the muscles showed rare gram-

7. Allen, Frank: Muscular Weakness and Hyperthyroidism: Myasthenia Gravis and Goitre: Case Report, S. Clin. North America **14**: 79 (Oct.) 1934.

8. Cohen, S. J., and King, F. H.: Relation Between Myasthenia Gravis and Exophthalmic Goiter, Arch. Neurol. & Psychiat. **28**: 1338-1345 (Dec.) 1932.

9. Wilks, Samuel: Guy's Hosp. Rep. **22**: 54, 1877.

10. Starr, M. A.: Myasthenia Gravis, J. Nerv. & Ment. Dis. **39**: 721, 1912.

11. Bell, E. T.: Tumors of the Thymus in Myasthenia Gravis, J. Nerv. & Ment. Dis. **45**: 130 (Feb.) 1917.

12. Norris, E. H.: Thymoma and Thymic Hyperplasia in Myasthenia Gravis with Observations on the General Pathology, Am. J. Cancer **27**: 421 (July) 1936.

13. Keschner, Moses, and Strouse, Israel: Myasthenia Gravis, Arch. Neurol. & Psychiat. **17**: 337 (March) 1927.

14. Butt, H. R.: Myasthenia Gravis, Arch. Path. **21**: 27 (Jan.) 1936.

15. Rosenow, E. C., and Heilman, F. R.: Bacteriological Studies in Myasthenia Gravis, Proc. Soc. Exper. Biol. & Med. **34**: 419-477 (May) 1936.

positive cocci, certainly having no anatomic relationship to the lesions noted, and we seriously doubt that there was any causal relation between the two.

All ductless glands were negative except for the thymus, which was extremely atrophic.

POSTMORTEM EXAMINATION

Unless specifically mentioned, the gross and microscopic appearances of various organs and structures were normal. The necropsy was performed four hours after death. The skin over the entire body was soft, smooth, slightly moist and waxy in appearance. There was a slight conjunctival hemorrhage near the inner canthus of the left eye. No palpable glands were present. The body was not excessively emaciated; the panniculus adiposus was 2 cm. deep and the abdominal and mesenteric fat was well preserved. The musculature throughout, including the diaphragm, was markedly thinned, the tissues appearing soft, flabby, friable and a very pale pink.

Heart.—This weighed 250 Gm. and was not particularly remarkable on gross appearance. There was little subepicardial fat. The myocardium was firm, nonfriable and a pale pinkish brown. The endocardium, valves and coronaries were normal. Microscopically the myocardium, particularly its outer half, showed marked changes. The muscle bundles showed little evidence of individual degeneration, the cross striations being well defined against a normal staining reaction. There was no cytoplasmic necrosis or vacuolation. The interstitial tissue was markedly edematous and widely separated the muscle bundles. It was infiltrated with large numbers of lymphocytes, occasional endothelials and rare neutrophils. Many areas of "lymphorrhagia" were present.

Lungs.—The right lung weighed 250 Gm., the left 220 Gm. They were not remarkable except for the bronchi, which were slightly reddened and covered with a thick, yellow tenacious mucopurulent exudate. Microscopically they showed an acute bronchitis and early bronchopneumonia. Interestingly enough, however, there were also a few scattered areas of loosely arranged fibrous thickening of the interalveolar walls, in which were accumulations of lymphocytes. These were more numerous than the customary lymphoid accumulations encountered in the lung and had no resemblance to healed tuberculous foci.

Spleen.—The spleen weighed 270 Gm. and was firm, smooth, regular and a dark purplish gray. On section the germinal centers were very prominent, standing out sharply as large gray dots 2 mm. in diameter against a depressed, moist dark crimson background which yielded no pulp on scraping. Microscopically the germinal centers were almost completely replaced by masses of infiltrating, phagocytic monocytes, while the surrounding pulp was heavily infiltrated with neutrophils.

Liver.—This weighed 1,470 Gm. and was essentially normal.

Gastro-Intestinal Tract.—The stomach showed a total absence of rugae. There was no thickening of the wall; the mucosa was intact. Microscopically there was slight chronic gastritis. The small intestine showed a few scattered patches of mucosal reddening, with no evidence of ulceration, induration or serosal involvment. Microscopically it showed an early acute focal enteritis.

Pancreas.—This weighed 100 Gm. and was distinctly swollen, soft and boggy. Peripancreatic tissue was edematous. Longitudinal section of the pancreas showed no evidence of fat necrosis or hemorrhagic pancreatitis. Milking the tissue brought small beads of yellow, purulent-appearing material to the orifices of the ducts. Microscopically the interstitial tissue showed multiple foci of acute inflammation in which no bacteria could be found. The other interstitial tissue was edematous but showed no general inflammatory infiltration, although minute foci of fat necrosis were present. The acinar and insular tissue showed no inherent abnormality.

Kidneys.—The right kidney weighed 120 Gm., the left 130 Gm. They were essentially normal.

Adrenals.—Together these weighed 20 Gm. They were normal in gross appearance. Microscopically they showed small areas of focal necrosis in the cortex, being invaded by neutrophils.

Genitalia.—These were essentially normal except for a few small follicular cysts of each ovary.

Aorta.—This presented very early atheromatous patches throughout.

Organs of the Neck.—The thymus weighed 5 Gm. It was extremely atrophic and on section presented a tough, yellow, fibrofatty appearing surface. Microscopically only the faintest scattered remnants of the original tissue remained, including rare lymphoid follicles and corpuscles.

Thyroid.—The thyroid weighed approximately 20 Gm. and was essentially normal. The parathyroids were essentially normal.

Striated Muscle.—Throughout the entire body the striated muscle was soft, flabby, friable and almost colorless, being a very pale pink. Microscopically sections through numerous muscles, including the diaphragm, all showed the characteristic picture theoretically associated with myasthenia gravis. The muscle bundles showed a marked variability in their size, shape and staining reaction. Some fibers were swollen to three times

Fig. 2.—Section of the thymus under low power showing marked atrophy; slightly reduced from a photomicrograph with a magnification of 25 diameters.

the dimension of others immediately adjacent to them. When so distorted, they presented the typical picture of Zenker's degeneration. In the majority of fibers the cross striations were well defined, but there was considerable tortuosity and irregularity of individual fibers. All fibers were widely separated by an edematous interstitial tissue heavily infiltrated with large numbers of acute and chronic inflammatory cells. Typical lymphoid accumulations or "lymphorrhagias" were present, as well as extensive general infiltration with lymphocytes and monocytes. Numerous foci of neutrophilic infiltration were present, in and about which were lacking any marked capillary engorgement or deposits of fibrin (fig. 3). Only the rarest gram-positive coccoid organisms could be found, and these seemingly had no relationship to any specific lesion, which gave the distinct impression of being artefactual.

CONCLUSIONS

From an exhaustive study of material at hand it must be concluded that one is dealing here with a case corresponding in general to the pathologic and clinical picture of myasthenia gravis. The reported accounts of the pathogenesis and characteristic changes of the

disease are so variable that one cannot be entirely sure of how accurately one's own observations correspond to the major concepts set forth by others. In this particular case there are no demonstrable pathologic changes of the central nervous system. The thymus is extremely atrophic instead of presenting hyperplasia or tumors, as described by many authors. With special stains we have been able to demonstrate coccoid bodies in some of the more severe lesions (pancreas, striated muscle), but we cannot demonstrate any immediate causal relationship between them and the pathologic changes observed, and they are not present in sufficient number, so that an artefactual basis might not easily account for them. We have noted, as have one or two authors, that there seems at least in places to be some perivascular involvement, although in our case

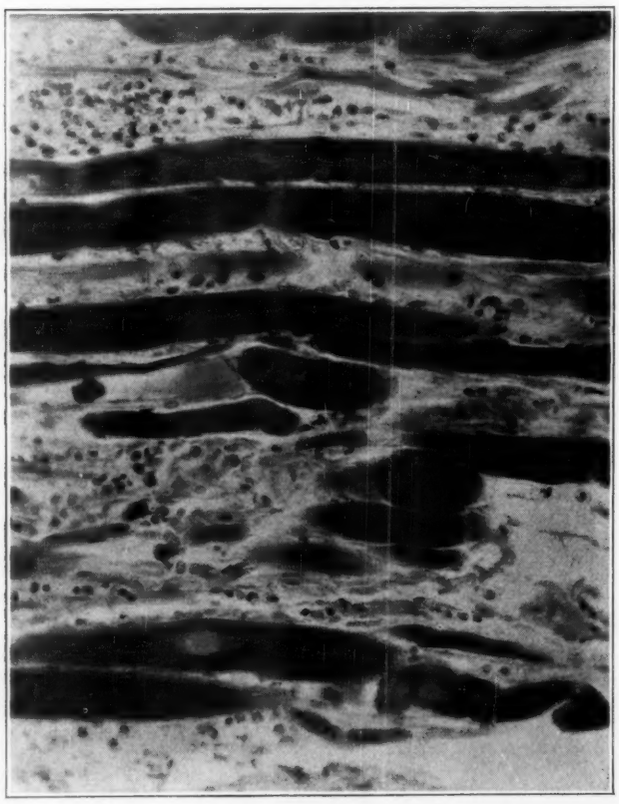

Fig. 3.—Section of the diaphragm, showing healthy and degenerating bundles. Interstitial edema and infiltration with lymphocytes and neutrophils (× 250).

this tended to be a phlebitis rather than an arteritis. The major finding, a well defined myositis affecting the striated muscles of the body, has been present throughout our case, the heart, muscles of locomotion and diaphragm all being markedly involved. The slight degree of acute bronchitis is almost certainly an insufflative terminal phenomenon. This is supported by the presence of large colonies of organisms within the bronchial lumens, while the immediately adjacent walls are entirely free from any inflammatory reaction. The small accumulations of lymphocytes scattered throughout the remainder of the lung seem to be slightly in excess of the normal disposition of lymphoid tissue in that organ. The acute splenitis, pancreatitis and enteritis and the focal necroses in the adrenal all seem to be terminal phenomena and certainly have little to do with the protracted course of the disease.

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PROBLEMS PRESENTED BY LESIONS OF THE RIGHT QUADRANT

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The diagnosis and treatment of lesions of the right lower quadrant do not as a rule present difficult clinical problems. But every so often patients with a disease condition in this region are encountered who not only have run the gamut of diagnostic procedures for years but also have undergone surgical intervention only to have a questionably diseased appendix removed.

In view of the fact that appendicitis is such a comparatively common disease, it is not surprising that the symptoms referable to the right lower quadrant are often ascribed to an inflammatory process of the appendix when in reality the lesion is in the cecum or the terminal part of the ileum. For example, it is a well known clinical observation that not infrequently patients with nonspecific granuloma or regional ileitis have an appendectomy performed and subsequently, when the symptoms recur, a pathologic process in the ileum is discovered. Patients with symptoms due to cecal stasis, spasm of the cecum or other lesions in this region are often subjected to the removal of the appendix only to have a recurrence of the clinical syndrome, perhaps in a more persistent form. The cecum may be the site of a benign or malignant tumor or an inflammatory or edematous process, infectious, parasitic or allergic in origin, which may give rise to a rather confusing clinical picture.

It is a fact that the usual physical and laboratory examinations do not always reveal the correct diagnosis. Special methods of investigation may be necessary, particularly a study of the small intestine. This diagnostic procedure has not been sufficiently utilized, although several observers [1] have stressed its clinical application. We have used it, with modifications, to diagnose lesions of the terminal part of the ileum and the cecum which were not detected by routine gastrointestinal examinations. In preparing the mixture for this investigation, four heaping tablespoonfuls of barium sulfate are emulsified in a quantity of cold water sufficient to fill a 10 ounce glass. Five or 6 ounces of this mixture is given for the oral method, while for the duodenal instillation 3 ounces is administered. Films are taken every one or two hours.

In the diagnosis of lesions of the right lower quadrant one must remember that the anatomic relationship of the viscera is such that the symptoms referable to this

From Lenox Hill and Beth Israel hospitals.
Read before the Section on Surgery, General and Abdominal, at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1937.

1. These include:
Mills, R. W.: Am. J. Roentgenol. **9:** 199-225 (April) 1922.
Forssell, G.: Fortschr. a. d. Geb. d. Röntgenstrahlen **37:** 393-394, 1928.
Morse, C. W., and Cole, L. G.: Radiology **8:** 149-153 (Feb.) 1927.
Cole, L. G.: Tr. Am. Gastro-Enterol. A., 26th Ann. Meet., Washington, 1933, pp. 240-250.
Cole, L. G., and others: Radiologic Exploration of the Mucosa of the Gastro-Intestinal Tract. By the Cole Collaborators, Milwaukee, Bruce Publishing Company, 1934, pp. 166-199.
Soper, H. W.: Radiology **20:** 76-78 (Feb.) 1933.
Ritvo, Max: Am. J. Roentgenol. **23:** 160-169 (Feb.) 1930.
Raiford, T. S.: Radiology **16:** 253-270 (Feb.) 1931.
Bloom, A. R.: Am. J. Cancer **18:** 296-317 (June) 1933.
Goldfarb, S. J.: New York State J. Med. **34:** 500-505 (June) 1934.
Kantor, J. L.: Regional (Terminal) Ileitis: Its Roentgen Diagnosis, J. A. M. A. **103:** 2016-2020 (Dec. 29) 1934.
Mackie, T. T., and Pound, R. E.: Changes in the Gastro-Intestinal Tract in Deficiency States, J. A. M. A. **104:** 613 (Feb. 23) 1935.

area may be due to lesions elsewhere in the body and that, conversely, general abdominal complaints or pain in the lumbar and sacral regions may be due to a pathologic process in the right iliac fossa. Furthermore, it is a fact that lesions of the right lower quadrant are not infrequently associated with other abdominal diseases or systemic infections.

In view of the foregoing facts it was thought of interest to report a series of cases, from both a medical and a surgical standpoint, of lesions of the right lower quadrant which presented various types of clinical problems. Gynecologic cases were not included in this study.

In the accompanying table we have summarized the case reports, emphasizing the use of the measures which were employed to detect and to treat the pathologic processes found. The following protocols are illustrative:

REPORT OF CASES

CASE 1.—L. D., a man, aged 41, first seen in June 1935, had a history dating back to 1918, when he had a severe attack of pain in the right lower quadrant, with cramps, while on the battlefield in France. He could not pass gas or have a bowel movement. The attack lasted for three days and was diagnosed as "acute appendicitis." No operation was done. In 1919 an appendectomy was performed in this country, when, after roentgenographic study, "chronic appendicitis" was reported. In 1921 a hemorrhoidectomy and in 1925 an operation for right inguinal hernia were performed. In 1932 the patient had a second severe abdominal attack similar to the one in 1918. Since then he had suffered many similar attacks, which increased in severity and were accompanied by frequent mucous stools. The results of numerous routine x-ray and laboratory examinations of all types, in many institutions, were reported persistently negative. Occult blood was found once in the stool. All observations pointed to "spastic colitis" and a large ampulla of the rectum.

In February 1936 a thorough roentgenographic study of the gastrointestinal tract gave similar results and in addition pointed to the possibility of some adhesions between the small

Fig. 1 (case 1).—*A*, four hour film, showing that the barium sulfate had stopped short at the ileocecal region. *B*, a six hour film, revealing a lack of proper filling in the lower portion of the cecum. In the upper portion the barium shadow shows quite a sharp cut-off at its base. Within the shadow there appear to be coils of terminal ileum.

intestine and the site of the operation for hernia. June 19, 1936, the patient experienced an exceptionally severe attack of pain in the right lower quadrant, although he did not report for examination until June 30. He had marked tenesmus and a slight mucous stool every fifteen minutes. Physical examination revealed a point of exquisite tenderness with rigidity midway between the appendical and the hernial scar. Subsequently tenderness was also elicited over the cecum and the ascending colon, where a definite doughy mass with borborygmi could be felt. The temperature and the blood count were normal. The stool showed a large amount of occult blood but no ova. The acute condition gradually subsided, leaving soreness and intermittent cramps, which the patient described as a stiffening of the intestine.

A study of the small intestine, oral method, was made on July 2, 1936, and this examination revealed the lesion (fig. 1). The preoperative diagnosis was intussusception of the terminal part of the ileum into the cecum, the probable activating cause

Fig. 2 (case 2).—Characteristic "string sign" of regional ileitis (Kantor[1]) after duodenal instillation of barium sulfate.

of which was a pedunculated tumor originating at the ileocecal junction. At the operation July 13 chronic intussusception, with a large papilloma of the cecum, was found. The terminal part of the ileum was also constricted. A one stage resection of the terminal part of the ileum, the cecum, the ascending colon and half of the transverse colon was performed with side to side ileocolostomy. The patient made an uneventful recovery, gained 30 pounds (13 Kg.) and is comparatively symptom free.

CASE 6.—B. T., a white man, aged 63, was well until four months prior to admission, Oct. 22, 1935, when he began to experience attacks of generalized cramplike abdominal pains, which bore no relation to food, did not radiate and were accompanied by nausea and constipation. He had lost 16 pounds (7 Kg.) during the preceding four months. Physical examination revealed a slightly distended abdomen, with a protuberant umbilicus; the liver was enlarged, but the spleen was not palpable. A nonmovable slightly tender mass was felt in the region of the cecum, over which there was a tympanitic note. The temperature did not go above 100 F. The laboratory examinations revealed a sedimentation rate of 105 mm. in forty-five minutes, hemoglobin 92 per cent, red cells 4,500,000, white cells 9,300 and polymorphonuclears 79 per cent (segmented 78 per cent). A roentgenogram of the colon, Oct. 25, 1935, revealed "a large tumor involving the cecum and the proximal portion of the ascending colon. The descending colon showed numerous large and small diverticula." A diagnosis of malignant growth was made. The surgical division, however, felt that the condition was inoperable.

The patient was treated medically by means of colonic irrigations, sedatives, antispasmodics and a bland diet. He began to improve and the mass in the cecum gradually disappeared, leaving a thickening of the walls. With this clinical improvement there was a gradual decrease in the sedimentation rate to 6 mm. in forty-five minutes. Another roentgenogram of the colon, taken Nov. 4, 1935, failed to show any evidence of the

Summary of Case Reports

Case	Diagnosis	Comment
1 L. D.	Intussusception of ileum into the cecum, with papilloma of cecum	Illustrates value of special x-ray studies of intestine as attack is subsiding but before it has entirely disappeared (fig. 1). Described in detail
2 L. M.	Regional ileitis	Illustrates the fact that by means of a special study of the small intestine a lesion can sometimes be definitely diagnosed; the patient, a woman, aged 22, had an appendectomy performed for attacks of pain in right lower quadrant of six months' duration; her symptoms recurred one and a half months after operation; routine x-ray studies gave negative results; a study of the small intestine (duodenal method) definitely revealed the lesion (fig. 2); resection was performed
3 E. F.	Diverticula of cecum and probable polyposis of terminal portion of ileum	In a patient with periodic attacks of pain in right lower quadrant diagnosed as "chronic appendicitis," a study of the small intestine (oral method) revealed diverticula of the cecum and small filling defects in the terminal portion of the ileum, which, owing to their circular shape, suggested a polypoid membrane; routine gastro-intestinal roentgenograms did not show the lesions (fig. 3)
4 N. L.	Adenocarcinoma of colon at ileocecal junction	Illustrates the fact that in a case of periodic attacks of abdominal pain and constipation a roentgenogram of the colon may not show any morphologic defect; a study of the small intestine (duodenal method) revealed typical step-ladder levels and marked dilatation of the coils of the small intestine; this pointed definitely to the presence of obstruction, which was diagnosed as due to malignant process; operation revealed an adenocarcinoma at ileocecal junction, which was removed in one stage (fig. 4)
5 C. D.	Adenocarcinoma of cecum	Illustrates the fact that malignant process in the cecum may resemble acute appendicitis; a woman, aged 55, complained of periodic attacks of cramps in right lower quadrant for two years; the attacks increased in severity, the last one being accompanied by nausea and vomiting; a hard, tender fist-sized mass could be felt in right lower quadrant; temperature 101 F., white blood cells 17,350, polymorphonuclears 90 per cent; a diagnosis of abscess in appendix was made; in the course of further questioning patient stated that at times she passed a considerable amount of bright red blood after colonic irrigations; this she attributed to hemorrhoids, which were present; after further questioning and physical examination, a diagnosis of carcinoma of cecum was made; operation revealed an advanced adenocarcinoma of cecum; anterior surface of cecum was so thin that only the serosa protected it from perforation; one stage resection with ileocolostomy was performed; patient made an uneventful recovery
6 B. T.	Diverticulitis of cecum	Illustrates the fact that an inflammatory process of the cecum may simulate malignant growth and also illustrates the diagnostic and prognostic value of the sedimentation rate of the blood; described in detail
7 R. F.	Acute intraperitoneal abscess, probably appendical in origin	Illustrates the value of thorough physical examination and the fact that in the presence of an acute inflammatory process, x-ray appearances may be misleading; described in detail
8 F. R.	Acute gangrenous appendicitis and choledocholithiasis	Illustrates the fact that, irrespective of previous operative observations and typical history, the patient with an acute condition in the abdomen should be most carefully examined for the possibility of acute appendicitis; described in detail
9 C. L.	Intestinal obstruction in terminal part of ileum due to gallstone	Illustrates the diagnostic value of a flat plate in diagnosis of an acute condition in the abdomen and correlating it with previous data and films; this procedure aided in making the preoperative diagnosis and helped to lessen the surgical risk; a roentgenogram of the gallbladder (without dye) in January 1932 revealed a large gallstone in a woman, aged 74; the patient had acute attacks of abdominal pain April 7 and was brought to the hospital April 14 with a clinical syndrome of intestinal obstruction; that day a flat plate of the abdomen showed that the stone was no longer visualized in the gallbladder region; a diagnosis of intestinal obstruction due to an impaction of the calculus in the terminal part of ileum was made and was corroborated at operation; through a McBurney incision with 0.5 per cent procaine hydrochloride anesthesia, the stone was found in the ileum and removed without difficulty by a simple enterostomy with primary closure (fig. 5)
10 A. F.	Perforation by foreign body of cecum, with extensive hyperplasia of adjacent lymph nodes	Illustrates the diagnostic problem presented by perforations of the cecum and the surgical procedure necessary; described in detail
11 M. O'C.	Postoperative adhesions around cecum and calculous cholecystitis	Illustrates the advantage of a thorough examination to reveal abdominal disease coexisting with a lesion in the right lower quadrant (fig. 6); described in detail
12 E. S.	Angioneurotic edema with visceral manifestations	Illustrates the diagnostic value of transitory eosinophilia in a patient with angioneurotic edema; the onset of the attack resembling appendicitis; described in detail
13 M. S.	Gastro-intestinal allergy with symptoms resembling appendicitis	Illustrates the fact that at times gastro-intestinal allergy may produce attacks resembling appendicitis; scratch tests revealed the allergens; described in detail
14 D. S.	Spasm of cecum due to a nutritional disturbance	In a patient on whom an appendectomy had been performed, followed by a recurrence of the symptoms, the finding of hypocholesteremia indicated the presence of an underlying nutritional disturbance; described in detail
15 A. R.	Spasm of cecum of undetermined origin	A roentgenogram with double contrast mediums, after atropinization, revealed a normal cecum although a diagnosis of malignant disease had been made by routine examination; patient has been symptom free since first observed two years ago
16 S. O.	Primary tuberculous retroperitoneal adenitis	Illustrates the fact that primary tuberculous adenitis must be considered when a small mass is palpable in right lower quadrant even though evidence of tuberculosis cannot be found elsewhere in the body; the history and physical appearances pointed to appendicitis, a large tuberculous node and the appendix were removed; subsequent treatment of the patient at the Finsen Institute and similar treatments in this country helped to restore her health and well being
17 M. G.	Tuberculosis of cecum and pulmonary tuberculosis	The lesion in the right lower quadrant was secondary to a focus in the lung; although patient had been treated for "colitis," a thorough examination revealed pulmonary tuberculosis with positive sputum; secondary tuberculosis of cecum was diagnosed by observation of tubercle bacilli in feces and by x-ray study
18 B. R.	Mucocele of appendix	In patients with history, typical signs and x-ray evidence pointing to a malignant process in the cecum, the presence of a movable tumor should make one think of the possibility of a mucocele of the appendix
19 J. D.	Inflammation of retrocecal appendix	While the history and presence of red blood cells in the urine indicated lithiasis of the urinary tract, careful examination determined the presence of an inflamed retrocecal appendix
20 W. W.	Regional ileitis with abscess formation and peritonitis	Illustrates how varied a clinical picture cases of regional ileitis may present; patient complained of abdominal symptoms for three years; at one time it was thought he had a peptic ulcer, and treatment for this gave him relief for one year; then his symptoms simulated nephrolithiasis and finally appendicitis; also illustrates the fact that in cases of ileitis at times only incision and drainage of the abscess are possible; an ileocolostomy was subsequently performed

previous tumor formation in the cecum but did reveal diverticula in the cecum, transverse colon and descending colon.

The patient made an uneventful recovery and left the hospital symptom free, with a diagnosis of diverticulitis, which probably was the underlying inflammatory process. What additional pathologic change caused the roentgenographic defect and the

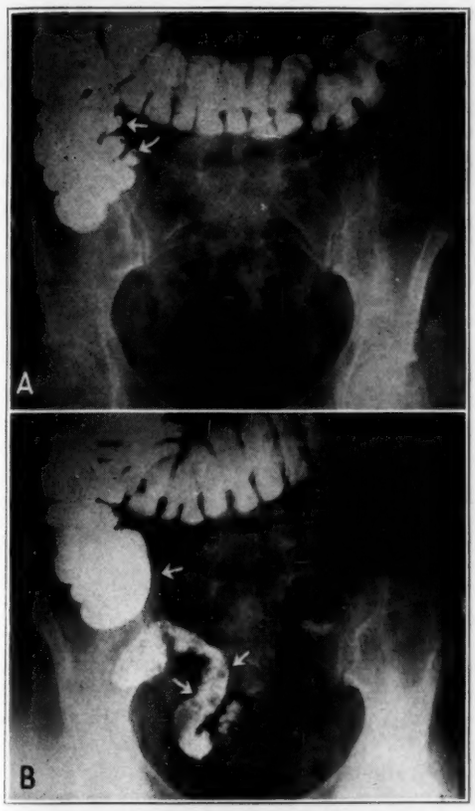

Fig. 3 (case 3).—*A*, diverticula of the cecum. *B*, small filling defects in the terminal portion of the ileum, which, owing to their circular shape, suggested a polypoid membrane. The appendix was also visualized.

mass, both of which subsequently disappeared, is problematic. We do know, however, that at times diverticulitis elsewhere in the colon may resemble a malignant disease. The patient was readmitted to the hospital Oct. 19, 1936, for a transurethral resection of the prostate gland, which was successfully accomplished.

CASE 7.—R. F., a white man, aged 64, complained of pain and a lump in the right lower quadrant of one week's duration, which, after x-ray examination of the gastro-intestinal tract, was diagnosed as an inoperable malignant condition of the cecum. The previous history was irrelevant except for a gastro-enterostomy ten years before for an ulcer of the stomach. On physical examination the patient was acutely ill, with generalized abdominal tenderness, moderate distention and an exquisitely tender mass in the right lower quadrant, which was not movable and did not cross the midline. Rectal examination revealed tenderness and bulging in the right fornix. When the examining finger was removed, gas was passed. The temperature was 101.8 F., and there were 13,400 white cells, with 80 per cent polymorphonuclears. The diagnosis was intraperitoneal abscess, probably appendical in origin. The operation showed a large abscess, with foul pus having a colon odor and with a thick edematous wall. The pathologic report was "chronic suppurative granulation tissue with no evidence of tuberculosis, syphilis or malignant change." The patient made an uneventful recovery.

CASE 8.—F. R., a white woman, aged 62, was operated on for calculous cholecystitis and choledocholithiasis Oct. 15, 1936. A cholecystectomy was performed, but, owing to the fact that the patient could not stand any further operative procedure, the stones in the common and hepatic ducts were not removed. After the operation the patient had three attacks of severe abdominal pain, the first and the second being accompanied by jaundice. Feb. 15, 1937, the patient had another attack, which at first was thought to be due to biliary calculi, as the others probably were. She did not improve. The next day she was brought to the hospital. Physical examination revealed marked distention of the abdomen, general peritoneal rebound signs and exquisite tenderness in the right lower quadrant. A tentative diagnosis of appendicitis was made and immediate operation was advised. Acute gangrenous appendicitis, with a walled abscess, was found.

CASE 10.—A. F., a white girl, aged 5, was referred to the hospital as having acute appendicitis on Feb. 20, 1923. Her chief complaints were pain in the lower part of the abdomen, occasional vomiting and fever of four days' duration. Examination showed an obliquely placed, elongated, firm, tender and nonmovable mass in the right lower quadrant. The blood count showed white cells, 35,000 and polymorphonuclears 89 per cent. During the next ten days the temperature and the pulse rate receded almost to normal. The bowels now moved regularly, but the mass remained unchanged. Roentgenograms showed outside pressure against the cecum and the ascending colon.

A tentative diagnosis of retroperitoneal lymphosarcoma was made and an operation performed on March 5. The tumor consisted of a large mass of lymph nodes between folds of mesentery extending from the hepatic flexure to 6 inches beyond the ileocecal valve. Side to side ileocolostomy into the midportion of the tranverse colon was performed. The lymph nodes removed at operation showed simple hyperplasia and edema with no evidence of tuberculosis or malignancy.

A second operation was performed two weeks later. The mass had decreased materially in size, and the site of the ileocolostomy had healed perfectly. At this time the mass and the involved portion of intestine were removed. Pathologic examination of the intestine and the tumor mass revealed acute suppurative colitis, with a perforation 2 cm. above the ileocecal valve, and lymphadenitis. The tract of the perforation was lined with granulation tissue and covered in places with cylindric epithelium derived from the mucosa of the intestine. In places, minute abscesses were present, and giant cells of the foreign

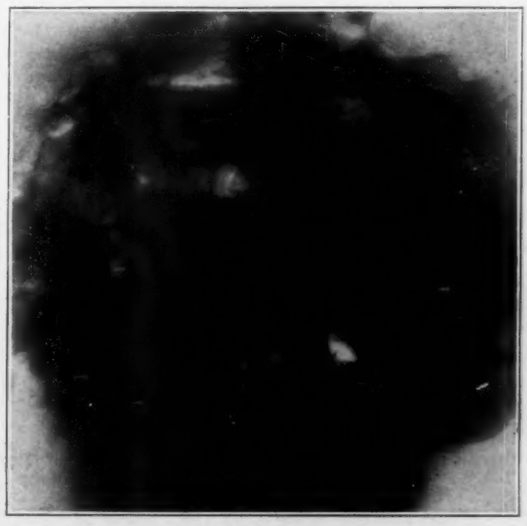

Fig. 4 (case 4).—Stepladder levels and marked dilatation of the coils of small intestine, after administration of barium sulfate through a duodenal tube.

body type were occasionally seen. The child has now grown into a perfectly healthy young woman, with normal bowel movements and normal general development.

CASE 11.—M. O'C., a white man, aged 42, gave the following history: In 1912 he was operated on for acute appendicitis and in 1915 for incisional hernia and was also treated for a peptic ulcer. About 1920 he began to have attacks of severe abdominal pain just above the appendix scar. The pain usually came on after eating; it started with a grinding sensation, radiated up to the right upper quadrant and was relieved by one or more

enemas. The attacks had been more or less constant the past five months. He was advised that the removal of some infected teeth would help him. The teeth were extracted, but the attacks continued.

While the present condition indicated an inflammatory or obstructive lesion about the cecum, the history and the radiation of the pain made an examination of the gallbladder and the gastro-intestinal tract advisable. Cholecystography showed a

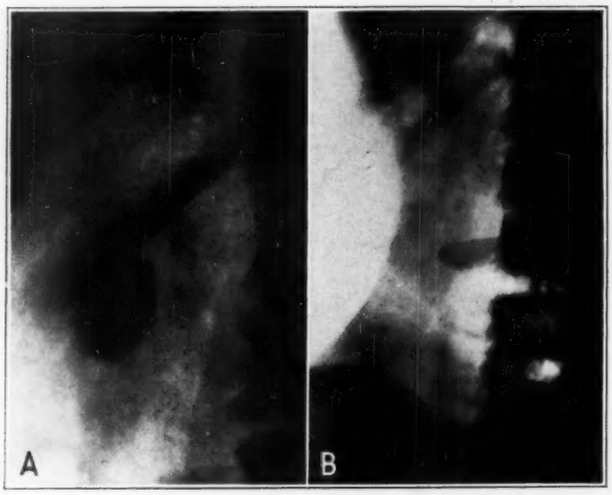

Fig. 5 (case 9).—*A*, large stone in the gallbladder (film taken without dye Jan. 11, 1932). *B*, stone no longer visualized in the gallbladder region (flat film of abdomen, April 14).

somewhat faint shadow with a mottled appearance, but a definite roentgenographic diagnosis of cholelithiasis could not be made. A series of gastro-intestinal roentgenograms gave essentially negative results. On aspirating the fasting stomach preliminary to a biliary drainage, numerous blackish particles were found. The microscopic examination of these particles showed numerous cholesterol crystals (fig. 6), the significance of which was emphasized by one of us in a previous article.[2]

A diagnosis of postoperative adhesions involving the cecum as well as calculous cholecystitis was made and surgical intervention advised. The operation revealed rather dense adhesions between the omentum and the anterior abdominal wall in the region of the old scar. There was also found a definite elongated strand holding the cecum to the anterior abdominal wall, with a large opening beneath it, which had allowed a loop of ileum to become caught in it. Two large stones and numerous blackish particles similar to those observed in the fasting gastric contents were found in the gallbladder. These particles were likewise composed of cholesterol crystals (fig. 7). A cholecystectomy, as well as a freeing of the cecum, was performed.

CASE 12.—E. S., a white man, aged 35, was perfectly well until three hours after eating corned beef and cabbage, when he was seized with severe generalized abdominal pain, accompanied by nausea and vomiting. The pain subsequently settled over the right lower quadrant. Tenderness was present over the appendix and the cecum, although no rigidity or muscular resistance was felt. The temperature was 99.5 F., and the blood count showed white cells 7,200, polymorphonuclears 60 per cent, lymphocytes 29 per cent, mononuclears 1 per cent and eosinophils 10 per cent. Although appendicitis was suspected, it was thought advisable to observe the patient further in view of the blood count and the absence of fever and local muscular resistance.

The next day the abdominal pain subsided and urticaria with giant hives appeared all over the patient's body. The eosinophils at this time dropped to 5 per cent. The following day jaundice developed, with the icteric index rising to 125. This jaundice was present for four weeks and was successfully treated by nonsurgical biliary drainage. The scratch tests never revealed any food allergens. The diagnosis was angioneurotic edema with visceral manifestations, as originally described by Osler,[3] who stated that in such cases a laparotomy was not infrequently performed.

CASE 13.—M. S., a man, aged 37, complained of periodic attacks of pain in the epigastrium which radiated to the right lower quadrant and which had been diagnosed as chronic appendicitis. The pain was followed in from one-half to one hour by a rash over the buttocks, which itched greatly. The pain and the rash usually lasted about ten or twelve hours. Scratch tests showed positive reactions to lettuce, celery, egg white, salmon, onions and tea. When the patient did not eat these foods, he was symptom free. Recently he was seized with a very severe attack in the appendical region followed by the rash. When he was seen the next day no evidence of appendicitis was found. On questioning it was learned that he had eaten onions the night before.

CASE 14.—D. S., a white woman, aged 29, first seen Nov. 28, 1932, had had periodic attacks of pain in the right iliac fossa for two years. One year before the appendix was removed in the hope that this operation would cure her. Six months later the pain recurred. She felt better when she ate strained vegetables, but as soon as she returned to a normal diet her pain recurred. The pain usually came on about four hours after meals and at times during the night. She was very constipated and had to resort to enemas. She also complained of dizziness, fatigue and headaches. Physical examination gave essentially negative results except that it showed tenderness over the cecum. The blood pressure was 100 systolic, 70 diastolic. The blood count and the urine were normal. The blood cholesterol content was 111 mg. per hundred cubic centimeters of blood. A series of gastro-intestinal roentgenograms revealed pylorospasm but no ulcer. A barium sulfate clysma showed evidence of spasm of the cecum and the descending colon.

Ultraviolet treatment and inunctions of hydrous wool fat to elevate the blood cholesterol were given as advocated by Leopold and Bernhard[4] and Berman.[5] A high vitamin, high caloric diet and irradiated oil orally and by rectum were also prescribed.

Fig. 6 (case 11).—Numerous cholesterol crystals, together with a slight amount of calcium bilirubinate pigment (preoperative specimen of fasting gastric contents).

The blood cholesterol content rose to 175 mg. per hundred cubic centimeters of blood. The patient has been symptom free since the treatment took effect.

COMMENT

Patients with lesions of the right lower quadrant not infrequently present varied clinical phenomena

2. Rafsky, H. A.: Am. J. Digest. Dis. & Nutrition **2**: 214-217 (June) 1935.

3. Osler, W. M. D.: On the Surgical Importance of the Visceral Crises in Erythema Group of Skin Disease, Am. J. M. Sc. **127**: 751-754 (April) 1904.

4. Leopold, J. S., and Bernhard, A.: Arch. Pediat. **46**: 756 (Dec.) 1929.

5. Berman, Louis: M. J. & Rec. **80**: 123 (Aug. 7) 1929.

which make them difficult diagnostic and therapeutic problems. In the main they may be divided into those with acute and those with chronic conditions. It is generally acknowledged that in most patients with acute symptoms referable to the right iliac fossa an inflammation of the appendix proves to be the etiologic factor. However, the principal diagnostic and therapeutic difficulties arising in patients with lesions of the right lower quadrant are usually encountered in patients giving a history extending over months or years. It is unnecessary to dwell on the errors made or on the needless exploratory operations so often performed. Doubtless most of us at some time or other have shared the responsibility.

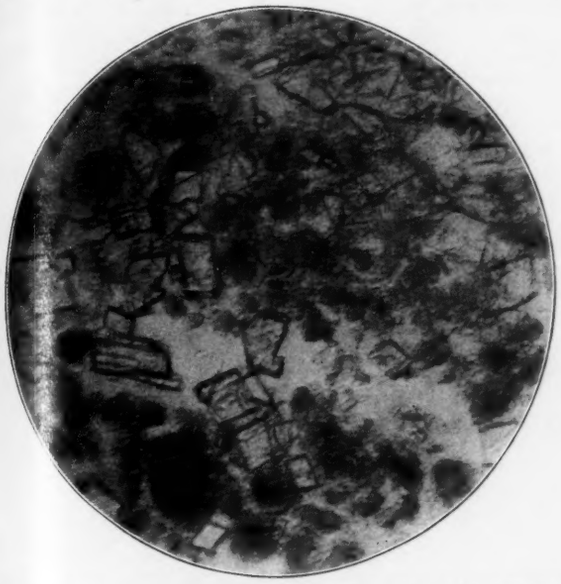

Fig. 7 (case 11).—Cholesterol crystals, together with calcium bilirubinate pigment (particle removed from gallbladder postoperatively).

We would, however, like to emphasize certain facts in connection with this paper. A careful and painstaking history and a thorough physical examination are still of paramount importance, even though marked progress has been made in the diagnostic aids which the laboratory has furnished. Furthermore, while an investigation of the gastro-intestinal tract by the usual routine procedures may reveal the lesion, negative results do not always rule out the existence of a pathologic process. Coexisting abdominal disease must also be borne in mind.

We do not believe in repeatedly subjecting the patient to the same gastro-intestinal studies when negative results are reported. Here special diagnostic procedures should be emphasized. A more frequent study of the small intestine as a means of detecting lesions of the terminal part of the ileum and the cecum should be encouraged.

The surgical treatment of lesions of the right lower quadrant will vary as to the pathologic process found. If, however, a definite preoperative diagnosis is made, the surgeon can map out a more comprehensive method of attack, his technic will be surer, surprise conditions at operation will be fewer and the risk to the patient will be much less. The presence of a diseased appendix always demands its removal.

At present there is no standard surgical procedure for the treatment of regional ileitis. The condition may present such varied clinical manifestations that it should be suspected whether or not the appendix has been removed. If the appendix is still present an appendectomy should be performed at the primary operation when feasible. If abscess formation is found, simple drainage is indicated. If marked inflammatory edema is present, an ileocolostomy, with short-circuiting of the affected part by means of healthy intestine well away from the lesion, is to be preferred, with possible subsequent resection. A primary resection is elected by some surgeons. At times an intestinal fistula then results, probably from lack of removal of all the affected area.

In cases of malignant disease of the cecum and the ascending colon, the presence or absence of edema and infection has a deciding rôle in the type of operation indicated. Our preference is for the one stage resection with ileocolostomy, when possible. If, however, this procedure is inadvisable, the two stage procedure is done or the operation as advocated by Lahey.[6]

All surgeons recognize the fact that marked inflammatory lesions in the ileum and the cecum may give a clinical and operative picture resembling malignant disease. Under these circumstances conservative surgical intervention is judicious.

SUMMARY

1. Lesions of the right lower quadrant often present diagnostic and therapeutic problems.

2. Special diagnostic methods are essential if routine gastro-intestinal examinations do not reveal a lesion.

3. Thorough study of the patient will prevent diagnostic errors and a needless exploratory operation.

4. Every lesion of the right lower quadrant does not necessarily require surgical treatment.

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ABSTRACT OF DISCUSSION

DR. ERNEST H. GAITHER, Baltimore: The information presented by the authors proves that if one is sufficiently versatile and persevering in the presence of atypical and puzzling syndromes, one will in most instances avoid the pitfalls which await the unwary whose first and last thought on the subject is that most lesions in the lower right quadrant are due to appendical involvement. My experience has been much the same as that of these contributors. In each case, the pathologic condition could easily have been discovered by interested and painstaking study of the symptoms, and application of clinical investigations which are available to all, and the patient might thus have been spared weary months of pain and discouragement. I am glad to say that after the discovery of the lesion each of these patients made a brilliant recovery. It would be most helpful to remember that a rich nervous supply places the alimentary tract and its changes under the influence of multitudinous impulses coming from all parts of the body. Hence it is most important to study each case in its entirety to distinguish between intrinsic abdominal disorder producing local symptoms, and extrinsic disease producing symptoms referred to various parts of the abdomen, notably the lower right quadrant. In this paper interesting instances have been presented of terminal ileitis, diverticula of the cecum, adenocarcinoma of the colon at the ileocecal junction, acute intraperitoneal abscess, acute gangrenous appendicitis, and choledocholithiasis, intestinal obstruction in the terminal ileum due to gallstones, and other lesions. It is this type of painstaking, investigative diagnostic acumen, which can be developed by all physicians, that leads to true progress in clinical medicine. That this progress in diagnostic certainty involves the amelioration of most of the ills of suffering humanity is not the least of our reasons for seeking to establish it.

6. Lahey, F. H.: Surg., Gynec. & Obst. **54**: 923-929 (June) 1932.

Clinical Notes, Suggestions and New Instruments

PELLAGRA SUCCESSFULLY TREATED WITH NICOTINIC ACID: A CASE REPORT

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AND
SUSAN GOWER SMITH, M.A.
DURHAM, N. C.

It is well known that liver and certain of its extracts are highly effective in the treatment of canine blacktongue and human pellagra. Recently, Mueller [1] and SubbaRow [2] have isolated nicotinic acid from liver. Elvehjem and his associates [3]

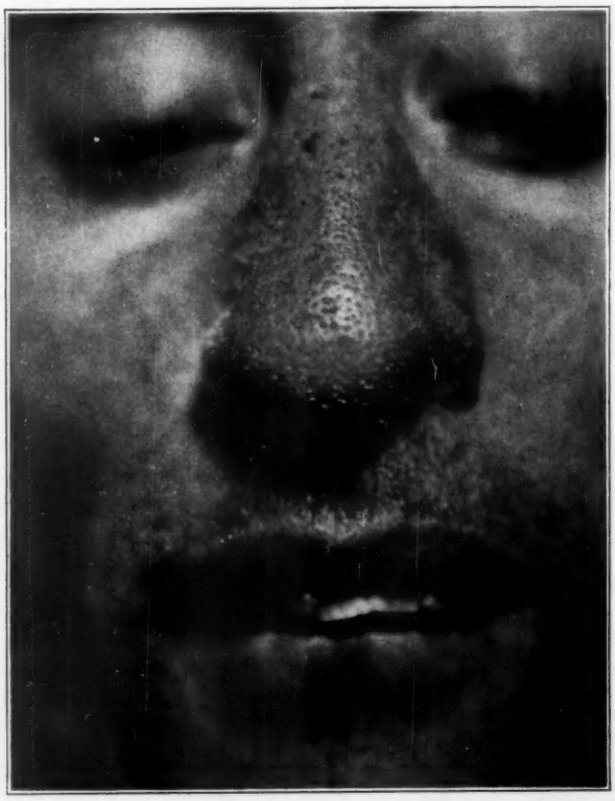

Fig. 1.—Horny concretions in the crifices of the sebaceous glands. The projections seen about the edge of the nose were present over the entire nose, face and forehead but do not appear in the rest of the illustration because they are out of focus.

isolated nicotinic acid amide from liver and showed that pure nicotinic acid (Eastman) would cure experimental blacktongue. This observation has been confirmed by Dann [4] and by Margolis and his co-workers.[5] The latter found that nicotinic acid in doses of 1.5 mg. per kilogram of body weight was highly effective in curing blacktongue in dogs, and harmless, whether administered orally, intramuscularly or intravenously. We have recently had the opportunity of using nicotinic acid in the treatment of a man with a very severe case of pellagra, with results so satisfactory that we feel that the case should be recorded.

REPORT OF CASE

W. H. B., a white male farmer, aged 42, weighing 41 Kg., was admitted to Duke Hospital Oct. 26, 1937, with a history of recurrent pellagra over a period of fifteen years. His present attack began in the summer of 1937 with glossitis, diarrhea, dermatitis and mild intermittent dementia. His diet has been grossly deficient but there was no history of alcoholism.

The patient was emaciated, dehydrated, chronically ill and intermittently disoriented. The tongue and buccal mucous membranes were slightly reddened but there was no definite papillary atrophy. A typical dermatitis was present on the hands and feet. The orifices of the sebaceous glands over the entire face were plugged with horny concretions (fig. 1). The remainder of the examination revealed nothing of significance except the absence of the abdominal and cremasteric reflexes. Hemoglobin was 13.6 Gm. (87 per cent); red blood corpuscles numbered 4,100,000. Urinalysis was normal. The electrocardiogram showed low upright T waves in all leads.

The patient was fed a basic diet [6] deficient in the pellagra preventive factor throughout his entire period of study. By the end of the first week it was obvious that he was becoming progressively worse. He refused to eat, became completely disoriented and developed delusions of persecution.

Treatment was limited to nicotinic acid (Eastman), the patient remaining on the basic diet. A solution was prepared in sterile physiologic solution of sodium chloride so that 1 cc. contained 2 mg. of nicotinic acid. On the seventh day after admission the patient was given intramuscularly 60 mg. of the drug. On the next day he received intravenously 60 mg. dissolved in 1,000 cc. of 5 per cent dextrose in saline solution. For the next six days he received 60 mg. daily, the intramuscular and intravenous routes being alternated. On one occasion he was given intramuscularly 60 mg. dissolved in 6 cc. of physiologic solution of sodium chloride. On two successive

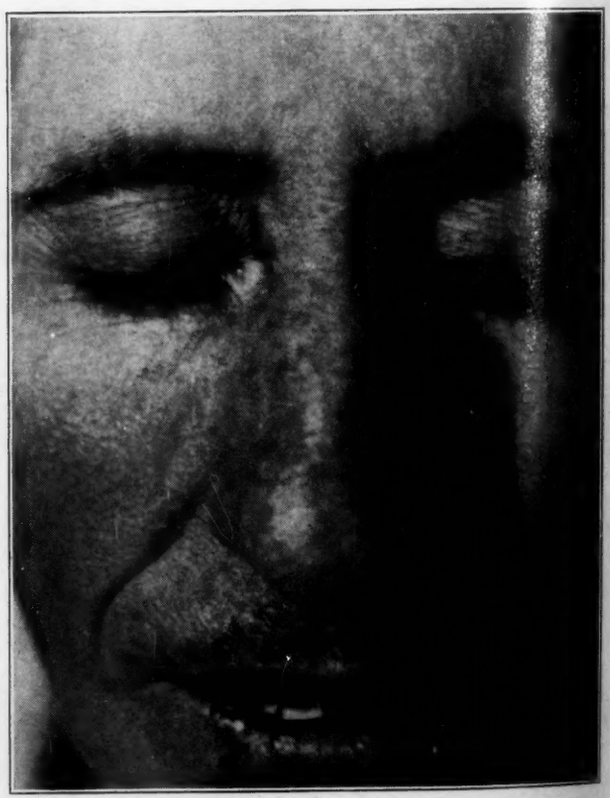

Fig. 2.—Same patient twenty days after photograph reproduced in figure 1 was taken and thirteen days after the beginning of treatment.

days 60 mg. was dissolved in 100 cc. of water and given orally. He was given in all 720 mg. of nicotinic acid.

No reaction followed the oral administration of the drug; however, a marked flushing of the face, neck, chest and arms appeared a few minutes after intramuscular injection and lasted for fifteen minutes. This same flushing was observed after the patient had received intravenously about 200 cc. of solution,

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or approximately 12 mg., but slowly faded even though the injection was continued. The pulse, respiration and blood pressure were unaffected and the patient experienced no discomfort except a slight feeling of warmth. The intramuscular injections were well tolerated even in high concentration.

The results of this treatment were dramatic. There was a striking improvement in the appetite within twenty-four hours. The mental confusion began to improve after forty-eight hours and he was entirely rational after six days of treatment. Within three days a definite change was noted in the appearance of the skin of the face, and after twelve days the skin was entirely normal (fig. 2). On the seventh day of treatment there was a striking change in the electrocardiogram, the T waves having returned to normal. On the twelfth day it was noted that the abdominal and cremasteric reflexes were present.

COMMENT

If subsequent investigations prove that nicotinic acid is the P-P factor of Goldberger, it would seem that the problem of the prevention and cure of pellagra have been greatly simplified. Nicotinic acid is very cheap; it cost less than 10 cents to treat this patient. It is possible that it could be mixed with table salt and sold in areas in which pellagra is endemic, similarly to the distribution of "iodized" salt in the districts in which goiter is prevalent.

SUMMARY

A patient who had endemic pellagra with anorexia, dermatitis, sebaceous gland changes and dementia made a dramatic recovery after the administration of nicotinic acid in doses of 60 mg. daily for twelve days.

MAGGOT THERAPY IN AN INFECTED WOUND IN HEMOPHILIA

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BOSTON

The treatment of infected wounds in hemophilia is a tedious process requiring caution because of the continual danger of hemorrhage. Certain medications, especially oxidizing agents, are frequently contraindicated because of this danger. Recently we have employed maggots in the treatment of a large infected wound in a severe case of hemophilia. The wound healed rapidly without hemorrhagic complications. The literature does not refer to maggot therapy in hemophilia.

REPORT OF CASE

I. G., a Jewish youth, aged 19, single, admitted to the hospital Jan. 18, 1937, complained chiefly of "swollen knees." The first evidence that he was a "bleeder" occurred at the age of 6 years, when a small cut on the buccal mucous membranes bled continuously for twelve days. The condition was diagnosed as hemophilia at that time. However, aside from a tendency to easy bruising and slightly prolonged bleeding from minor injuries, he remained free of any critical episodes until the age of 13 years. The temporary teeth were lost without excessive hemorrhage except in one instance. For the past six years he had had frequent hemarthroses involving the knees, ankles and elbows. Five years before admission an attempt to correct forcefully a flexion deformity of the left knee resulted in severe hemorrhage, which was controlled only after three blood transfusions. Shortly after this a hemorrhage developed in the muscles of the left calf. The skin broke down over the posterior aspect of the leg and an extensive infected wound followed. Although under constant care of physicians, this wound did not completely heal for one year. Two years before admission the patient suffered from renal pains and there was hematuria on two occasions. There has been no hematemesis, melena, hemoptysis or epistaxis. He had had repeated hemorrhages into both knee joints for the past six months and had not walked for five months. He had scarlet fever in a mild form without complications four years before admission. The weight had remained quite constant at 150 pounds (68 Kg.) for seven years. The family history is completely known up to and including the four grandparents and is negative for hemophilia. The mother died at the age of 50 of agranulocytic angina. The father, aged 58, is living and well. The patient has one brother, aged 29, living and well and without bleeding tendencies. He has one sister, aged 33, who is married and has three sons and one daughter, none of whom display a hemorrhagic tendency. All have normal blood coagulation times. The mother of the patient had one brother and two sisters. One of these sisters has a son who is not a "bleeder." All four grandparents are deceased and none are known to have had abnormal bleeding tendencies.

On physical examination the patient was well developed and well nourished. The head, eyes, ears, nose and throat were normal except that the tonsils were enlarged and cryptic. The lungs were clear and the heart was normal. The blood pressure was 128 systolic, 80 diastolic. Nothing abnormal was found on examination of the abdomen, genitalia or rectum. Neurologic examination was negative. Both knee joints showed a moderate effusion with restricted motion because of pain. There was a linear white scar 15 cm. in length on the left calf, which was bound to the underlying tissues. The muscles of the right calf were hard and indurated as a result of an old intramuscular hematoma.

On admission the red blood cells were 5,140,000 per cubic millimeter, hemoglobin 14.5 Gm. per hundred cubic centimeters, and the hematocrit reading 42.1 per cent. The white blood cells were 8,150 per cubic millimeter and the differential count was normal. Urinalysis and examinations of the stool revealed nothing abnormal. The Hinton test of the blood was negative. The coagulation time, determined by placing 2 cc. of venous blood in a 100 by 13 mm. test tube at 37.5 C. was 125 minutes on admission. Clot retractility was normal. The bleeding time was two minutes (Duke's method). The platelet count was 302,000 per cubic millimeter. The patient's blood group was B. X-ray examination of the knees showed a chronic degenerative arthritis.

The patient was confined to bed and the knees were treated with radiant heat and active and passive exercises. February 4 there was a spontaneous recurrence of hemorrhage into the muscles of the right calf. The leg was elevated, immobilized and packed with ice. Opiates were required for the relief of pain. The bleeding was apparently stopped by two transfusions of whole citrated blood, 300 cc. twenty hours after the onset of hemorrhage and 200 cc. twenty-four hours later. At this time the right lower leg was approximately three times larger than usual. As a result of circulatory stasis a marked edema developed in the right foot and ankle. The sensations and temperature of the foot remained normal. An ecchymotic area developed over the popliteal space. Several large blisters containing brown fluid formed over the posterior aspect of the leg. As a result of the hemorrhage the hemoglobin dropped from 14.5 to 9.2 Gm. per hundred cubic centimeters in spite of the two small blood transfusions. The icterus index temporarily rose to 10. The anemia decreased with iron therapy.

The leg was dressed with sterile precautions daily and care was taken to avoid pressure over the tensely swollen portion. The blisters did not rupture until the twelfth day after the hemorrhage. From this time the open lesions continued to discharge large amounts of blood-tinged serous material. In spite of various local treatments a deep denuded area measuring 6 by 15 cm. developed over the calf region. There was a smaller lesion 2 cm. in diameter in the popliteal space that refused to heal. Both lesions were filled with old blood clots and a low grade infection was present. It was felt that the breakdown of tissue was due to pressure necrosis from the inside. Because of a 25 degree flexion deformity of the knee and a weakness of the dorsiflexor muscles of the right foot, baking and massage were started to the knee and electrical stimulation was begun for the drop foot.

Because of the lack of healing in the infected wounds and a daily fever of from 100 to 102 F., maggots were first placed in the wound five weeks after the hemorrhage. Dressings were changed daily and additional maggots added as necessary. During the next week all the old blood clot and much of the necrotic material had been removed by the maggots. The temperature dropped to normal. The gastrocnemius muscle was exposed and the wound at this time measured 4.5 cm. in depth. It was undermined from 3 to 5 cm. in all directions.

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Maggot therapy was continued for four weeks. The skin layer healed to the muscle tissue, leaving two long narrow sinuses. Healing might have been hastened if it had been feasible to expose these sinus tracts surgically. Nevertheless, during the four weeks that the maggots were used, the infection entirely cleared up and the wound healed rapidly. At the end of this period a clean granulating area measuring 1 by 5 cm. remained. This healed completely in two weeks with the application of warm boric acid packs. At no time during maggot therapy was there any evidence of bleeding, although the healing tissue was extremely vascular. Throughout this period the coagulation time of the blood was never less than two hours and varied between 122 minutes and 188 minutes. The patient became ambulatory and was discharged from the hospital May 8.

SUMMARY

In a case of hemophilia with an extensive wound resulting from necrosis of a hematoma maggot therapy was used with rapid clearing of the infection and resultant healing without any complicating hemorrhage. Five years before this patient had an almost identical lesion on the opposite leg resulting from the same cause. This wound did not completely heal for one year, while the lesion reported here healed in three months. Apparently maggot therapy may be used in wounds in hemophilia, after the cessation of active bleeding, without danger of hemorrhage.

Special Article

POSTGRADUATE INSTITUTE ON PNEUMONIA

Held at Rochester, N. Y., Oct. 19, 1937, Under the Auspices of the Medical Society of the State of New York and the New York State Department of Health

The Early Clinical Diagnosis of Pneumonia

DR. WILLIAM S. MCCANN, Rochester, N. Y.: Recent advances in the treatment of pneumona yield dramatic results with certain types of the disease, notably type I. In the records of the Strong Memorial Hospital, cases of type I pneumonia treated in the first ninety-six hours had a mortality rate of only 11 per cent as contrasted with 44 per cent in cases treated later than ninety-six hours, and 54 per cent of all cases of pneumonia in which specific treatment was not given. The advantage of beginning treatment on the first day is clearly apparent in figures showing a rising mortality rate for each day that treatment is delayed. This makes the value of early diagnosis unquestionably important. Early diagnosis is important apart from the question of serum treatment, because pneumonia is a contagious disease in which no time should be lost in applying measures to prevent the spread of infection.

Signs of consolidation in the lung are almost never present at the onset and may not be present in characteristic form for from twenty-four to forty-eight hours or even longer after the onset. In textbooks the sudden onset with a chill is greatly emphasized. While this is usual and characteristic of at least two thirds of the cases, in many others a sharp chill may be missing. It should also be borne in mind that pneumonia in elderly and debilitated persons may be almost afebrile. In a typical case the early diagnosis rarely presents much difficulty. The sharp onset, with rigor, rapidly rising temperature, pain in the side, cyanosis, inspiratory dilatation of the alae of the nose, dyspnea, labored breathing with pain in the side and cough, produce a picture which instantly calls lobar pneumonia to mind. In less typical cases the respiration ratio may give the principal clues to invasion of the lung. Normally the ratio of pulse rate to respiration is 4 to 1. A change in this ratio from 3 to 1 or 2 to 1 is, to my mind, the most constant of the initial phenomena of the disease. The breathing is not only rapid, it is shallow; inspiration seems to be checked short, and the sudden release of expiration may produce a slight grunting sound. Coincident with the appearance of rapid shallow breathing, cyanosis becomes obvious in the lips, ear lobes and finger tips, and usually in the cyanotic flush of the cheeks. Pain in the side may give early indication of the part of the lungs involved, and limitation of respiratory movement on the side involved is an early phenomenon. The decubitus is important. The patient tends to lie on the side of the invasion and almost invariably lies flat. The presence of orthopnea is presumptive evidence against the diagnosis of pneumonia. In such a case the true diagnosis is far more likely to be infarction of the lung. The percussion note and fremitus rarely give consistent evidence during the stage of invasion of the lung. On auscultation the breath sounds over the involved areas may show simply a diminished vesicular murmur, later complete suppression of the breath sounds over certain areas, with bursts of fine crepitant râles on inspiration after cough.

The important early clues to a diagnosis of pneumonia, I would list in the order of their constancy and reliability as follows: 1. Character of breathing: dilated alae on inspiration; rapid, shallow expiratory grunt; low pulse respiration ratio, 3 to 1 or 2 to 1. 2. Cyanosis. 3. Dyspnea, cough, pain in the side. 4. Localized limitation of respiratory movements with suppression of breath sounds and frequently fine crepitations. 5. Character of the sputum: blood cells and leukocytes and pneumococci. 6. Onset with rigor. 7. High degree of leukocytosis. Pneumococci of type I or type II are rarely present in healthy persons. When these types are found in blood tinged sputum there is little reason to doubt the existence of a pneumococcic infection. Organisms of type III and group IV are not uncommonly found in the throats of healthy persons. Their presence in sputum has less significance as primary causative agents in pulmonary disease. In my opinion, x-ray examination is of little value in the early diagnosis of pneumonia. It may be important in differential diagnosis in doubtful cases and special conditions which I shall refer to under differential diagnosis. In true pneumococcic pneumonias the use of the x-ray examination is quite superfluous in the early stages, and valuable time should not be wasted on it as a rule.

As the invasion of the lung progresses, the typical signs of consolidation may be heard at the periphery of the lung in one part sooner than another. Before frank signs of consolidaton appear, however, dulness may increase, the character of the whispered voice transmission assumes a bronchial quality, and the râles heard have a consonating quality and seem to be close to the ear. In case of invasion of a new lobe when one lobe is already consolidated, the temperature, which has been previously elevated, may drop for a few hours. During this drop the patient exhibits some evidence of shock, the pulse may accelerate, the blood pressure fall, the respirations increase. Cyanosis returns. Suppressed breathing and râles may recur over the new lobe. The temperature after a temporary fall rises again. When such evidence of new invasion occurs, the sputum should be retyped. Necropsy sometimes reveals different types of pneumococci in different lobes. This should remind one that patients with pneumonia should be protected from infection with other types of pneumococci introduced by visitors, attendants or nearby patients and make one alert to use specific serums on bacteriologic evidence obtained at each new lobar invasion, whatever the initial type of pneumococcus.

Too much effort should not be wasted in differentiating between lobar pneumonia and bronchopneumonia. A common mistake is to confuse large pulmonary infarcts with lobar pneumonia. The points to remember are that infarcts of the lung are usually found in orthopneic patients. The sputum with infarction is frankly bloody from the start. Fever, leukocytosis and signs of consolidation occur with infarcts, and the physical signs develop more rapidly than in pneumonia. Cyanosis is usually more profound than in a pneumonia with corresponding amounts of consolidation. The diagnosis usually depends on recognition of the associated heart disease or phlebitis from which the infarction originates, and the coexistence of orthopnea should always raise doubt if a diagnosis of pneumonia has been made. The differential diagnosis between pneumonia and pleural effusion occasionally gives trouble. In case of doubt, aspiration with a needle will settle the matter. Fluid displaces the heart to the opposite side; massive atelectasis displaces the heart toward the atelectasis. Massive atelectases may be accompanied by pneumococcic infection. I have seen three type I pneumonias with atelectasis occur in the same lobe in a man with aneurysm and compression of the bronchus to the lobe. In case of doubt between massive atelectasis or pleural effusion

and pneumonia it is always safe to study the sputum and give serum if a specific type I or II pneumococcus is present. The discussion of differential diagnosis should not overlook the signs of consolidation frequently found in the lung in acute rheumatic fever. These arise in several ways: (1) by compression of the left lower lobe posteriorly by fluid in the pericardial sac, (2) by pleural effusions and (3) by rheumatic arteritis with congestion and atelectasis. There is no such thing as rheumatic pneumonia. Here again doubt will be resolved by study of the sputum itself and by recognition of other features of acute rheumatic fever. In differential diagnosis chest roentgenograms may be of use. Recourse to roentgenology may be had at any time. However, I cannot visualize a situation in which it would take precedence over a careful physical examination and the study of the sputum itself. The collection of sputum is occasionally difficult. In children it may not be expectorated. It is frequently possible to get it on a piece of sterile gauze over a gloved finger inserted well back in the pharynx. In this discussion I have not emphasized the importance of taking a blood culture. I do not mean to convey the idea that I regard blood cultures as of little value. Quite the contrary. I have been more concerned with the early phenomena which would lead to suspicion of pneumonia and which would lead the physician to have sputum and blood culture done, leaving the discussion of these procedures to the next speaker.

DISCUSSION

DR. EDWARD S. ROGERS, Albany, N. Y.: All are probably aware that in connection with the pneumonia program of the Bureau of Pneumonia Control of the State Department of Health for the past two years there has been a fair amount of general lay educational activity. We are not, of course, attempting to teach the public how to diagnose pneumonia. We do feel that before the methods of treatment which we have can be applied we must be reasonably sure that laymen will consult the physician early in the disease. Therefore we have selected that group of symptoms which are more typical and which the layman should be able to recognize; namely, the chill, pleurisy, rusty sputum and fever. Any one of these four, we are telling them today, are of themselves sufficient indication for calling a physician at once. We are laying particular stress on the development of these symptoms with a preceding story of upper respiratory infection.

The Bacteriologic Diagnosis of Pneumonia

DR. J. D. GOLDSTEIN, Rochester, N. Y.: The pneumococcus causes by far the majority of all pneumonias. A discussion of the etiology of the pneumonias implies a discussion primarily of the pneumococcus. Morphologically the pneumococcus is a gram-positive ovoid organism which on the stained slide may appear in pairs or in short chains. Originally the pneumococcus was put in the streptococcus group, and as it is examined under the microscope one may not be able to differentiate the two. There are, however, certain bacteriologic criteria by which this differentiation can be made. One is the presence of a capsule on the pneumococcus; the other is that the pneumococcus is bile soluble. In addition, it is possible to recognize the organism by its colony growth on blood agar. It is known that pneumococci differ antigenically; in other words, there are different types of pneumococci. This was suggested over thirty-five years ago by Neufeld. With the impetus of the large number of pneumonias seen during the war period, Dochez and Avery were able to separate out three definite types; I, II and III, and a large group, the so-called group IV, in which were placed all those not in the first three types. From 1929 to 1932 Dr. Georgia Cooper and her associates defined twenty-nine types of pneumococci in group IV. These types were just as distinct as the previously recognized types I, II and III. There is a very small amount of crossing of these types, as, for instance, between types III and VIII, II and V, VII and XVIII, and XV and XXX. This crossing is not of significance, as the methods of identifying the separate types are adequate to differentiate them.

The classification depends on the type of carbohydrate substance which the organism contains. This carbohydrate is present in the capsule. The details of this phase of the problem were clarified through the work of Heidelberger, Goebel and Avery. It is known now that the pneumococcus contains two fractions: the carbohydrate fraction contained in the capsule and the protein fraction in the body of the organism. Type specificity depends on the carbohydrate substance in the capsule. The distribution of pneumococci is of importance. In different years one will find a preponderance of a particular type of pneumococcus. The preponderant type will also vary in different communities in the same year. In Rochester we have a list of 805 typings from October 1935 to October 1936, and from this table one can get an idea of the distribution of types for this period. During this period type I was found ninety-one times, type II fifty-nine times, type III 162 times and all others 493 times. In general, it is worth noting that between 55 and 60 per cent of pneumonias are usually due to types I and II, about 35 per cent of type I and from 20 to 30 per cent of type II.

Pneumococci of types I and II are rarely found in the throat of a normal person. This, however, is true only in a limited sense. Types I and II and other types of virulent pneumococci are found in the throats of many normal persons who have been in contact with known cases of pneumococcic infection—not only of lobar or bronchial pneumonia, but of any type of pneumococcic infection. The discussion as to whether or not there is a carrier stage has been answered definitely. Carriers of virulent pneumococci do exist, usually in contact with a known case of pneumococcic infection.

One must know the type in order to be able to use the serum that is indicated. That is the obvious reason for the importance of typing. The importance of early typing will be just as obvious from the following papers and from what Dr. McCann mentioned. The mortality is directly in relation to the speed with which one gets serum to the patient. This has been statistically proved repeatedly, and I think it can be said that it is an accepted fact. If serum is given early, good results will be obtained.

Occurrence of the Various Types of Pneumococci

Type		Type		Type		Type	
I	91	IX	18	XVII	22	XXV	13
II	59	X	7	XVIII	10	XXVII	3
III	162	XI	13	XIX	28	XXVIII	4
IV	13	XII	21	XX	20	XXIX	20
V	36	XIII	14	XXI	9	XXX	16
VI	26	XIV	18	XXII	11	XXXI	19
VII	27	XV	5	XXIII	10	XXXII	28
VIII	64	XVI	5	XXIV	13		
Total							805

What about the methods of typing? Since 1902 a method has been written into the literature which is now preferred. Neufeld in 1902 wrote that when a pneumococcus is injected into a rabbit and an antiserum is produced, and then the pneumococcus is mixed with the serum, the pneumococcus changes in appearance by becoming much swollen. He was able to identify the organism by this reaction. In 1932 Armstrong, Logan and Smeal in England and in 1933 Sabin in this country again worked with this technic, the so-called Neufeld or quellung reaction. It is a simple test: a drop of sputum, a drop of dye and a drop of serum examined microscopically. The preparation is examined in five or ten minutes and one either does or doesn't see the reaction. It is specific. It is 90 per cent efficient, as checked by the reliable and relatively absolute mouse method.

What procedure should one follow when a person suspected of having pneumonia is admitted? This may be heresy, but I say that to do typing alone and depend on the quellung reaction alone requires a certain amount of unjustifiable courage, particularly if one is not acquainted with the test. The people who work in laboratories expect an error of from 5 to 10 per cent in working with the quellung reaction. They check themselves by repeating the test and by further procedures. Therefore the ideal thing to do with a sputum specimen is to send it to a laboratory, which is best equipped to do this type of work.

We use a blood culture as a reasonably good prognostic index, and we use the blood culture as a reasonably good

criterion for the intensity of treatment. We don't always think of it as a typing method, yet it may be the only method that will work. One other important advantage about the blood culture should be obvious; when one has a type III sputum report and a type I blood culture report, obviously one thinks of and uses the type I serum. Mixed infections do occur. A mixture is not infrequent. The blood culture is obviously of importance as a typing method as well as a prognostic index. A thick, glairy, tenacious, slightly blood tinged sputum is best for a quellung reaction. In some patients one does not get sputum. The thing to do is to swab the throat as thoroughly as one can and see if coughing can be induced. In children it is worth remembering that sputum is swallowed and occasionally the stomach tube will produce a suitable sample for typing. One should get whatever sample one can and by all means persist in trying to get the sample. Speed is obviously essential, and the best way to get speed is to take advantage of the nearest laboratory. A blood culture should always be used. Finally, it is worth checking the typing. Our quellung reactions are checked by the macroscopic tube method. We find discrepancies. Not only will one check the inaccuracies of the laboratory by sending in a second sample of sputum, but there are mixed infections which may be so clarified.

DISCUSSION

DR. ROGERS: I think that probably all physicians have at their command many ways of treating pleural pain. Any means of relieving pleurisy enough so that the patient can make the necessary effort to cough up a good specimen will pay one for time and effort. Why do I say this? Because if one has to resort to taking a blood culture it will take from six to eight hours, probably, to get a report. Therefore, two or three hours spent in trying to get a sputum specimen would be to the advantage of the physician and of the patient. Furthermore, one can place more reliance on the report of the sputum specimen. On the use of opiates, opinion is somewhat divided. I think that early in pneumonia the discreet use of codeine to relieve pain may be justifiable. The use of morphine has came in for a great deal of criticism, probably well founded. Another point of practical importance is that if one has a specimen, particularly in the middle of the night, one will save time by telephoning the laboratory from the patient's house before sending the specimen. The principal sources of error in typing are not going to be in positive reports from the laboratory but in negative reports. I think one might well say beware of a group IV report. If it is group IV and one has a typical case of lobar pneumonia, it is well to repeat the typing, because the typical case of lobar pneumonia is more liable to fall in those types for which we have serum. If the report is negative or inconclusive, it probably means that the laboratory did not receive a satisfactory specimen. Of course that calls for another specimen. The two together—serum and blood culture—provide the most accurate method generally available of typing, barring perhaps lung suction, which is not generally applicable outside certain clinics. As a result of our first two years' study we found that if all the type I cases which had blood cultures were done in hospitals, only 30 per cent of the type I pneumonias in hospitals are having blood cultures. That offers us a point to develop our blood culture work. Just what the answer to that is, I don't know. I put it up to you as somewhat of a question, and your thoughts on it will be more than welcome.

Oxygen Therapy of Pneumonia

DR. J. G. M. BULLOWA, New York: Not every patient requires oxygen, but there are two reasons for its use. In the first place, the patient who has pneumonia has a fever and needs more oxygen. The patient with a fever of 104 or 105 needs one and a half times as much oxygen as one resting quietly in bed with a normal metabolism. Then there is another reason. Ordinarily 80 square meters of capillary surface is exposed in the alveoli. When the lung is consolidated there is less surface. One of the methods of showing this want of oxygen is by cyanosis. Many patients recover without oxygen, but anoxemia increases the hazard of pneumonia and the prognosis becomes distinctly worse. Under these circumstances how can one get more oxygen into the blood? If one wants to get more water out of a faucet than is able to pass through at a given pressure, one can increase the pressure. That is exactly what we do when we give oxygen. We increase the pressure of the oxygen at the interface. We give oxygen when there is an increase in the pulse rate, an increase in the respiratory rate or an increase in the nervous irritability. At Harlem Hospital, where we cannot always observe the capillaries of the skin, we give oxygen when the pulse becomes 120 or when the patient is nervous and irritable.

Intravenous oxygen is dangerous. Subcutaneous oxygen is inefficient. It can be given with a catheter, a method which has many objections, although a catheter or rubber tube is always at hand. Then one can use an inhaler, a pronged metal inhaler which just fits within the nostrils. Another method is to use a mask which fits about the face. Finally, one can use either a tent or a chamber. Each of these methods has its place. Ordinary industrial oxygen, best taken from the ordinary industrial tanks, is needed. A gage is needed to show the rate at which the oxygen is being delivered. Finally, one needs to know whether there is any oxygen remaining in the cylinder. There is also needed a method of moistening the oxygen, because dry oxygen is irritating to the nasal mucous membranes. How high must the gradient be in order that we shall have efficient oxygen therapy? All I can say is "enough," because what will be adequate for one patient will be utterly inadequate for another. Ordinarily the gradient is about 70 mm. of mercury. That is partial pressure. We can lower the need for oxygen by lowering temperature either by skilful nursing, which means more rest, or even by the use of antipyretics, or we can supply enough oxygen. Ordinarily the venous blood contains 5.5 per cent, or 40 mm. partial pressure of oxygen, and the arterial blood 13.42 per cent, or 100 mm. of pressure. In this room it is 21 per cent, or 160 mm. In the alveolar air it is 14.5 per cent, or 110 mm., so that the respiratory gradient is the distance between 110 and 40. In the expired alveolar air, when oxygen is being supplied by a nasal catheter at the rate of 4 liters a minute, there is 30 per cent oxygen in the alveolar air, or a pressure of 226 mm., and the respiratory gradient becomes 166 mm. as opposed to what it was before, which was 70 mm. If a much more rapid flow, 80 liters a minute, is being used, the normal gradient has been increased at least fourfold. Oxygen in an ordinary commercial cylinder is adequate. There is no medical oxygen. Regulators are important, and there are two types. One type has a variable orifice and the other a fixed orifice. There are two ways of giving oxygen directly from the cylinder. There is a device which takes the oxygen just inside the nostrils, and there is the catheter which carries the oxygen into the pharynx. Even writers who are most enthusiastic for the catheter admit that in 15 per cent of the cases they are unable to use it because the patient gags and rejects it. Patients do not reject the inhaler, because of the difference in the point at which the oxygen is discharged. Oxygen is accepted more readily when it is delivered to the mucous membranes of the nose rather than in the pharynx because the impact depends on the resistance and the size of the opening. It makes a difference whether the inhaler discharges the oxygen close to the mucous membranes or at a distance of 1 inch or an inch and a half, because the pressure rapidly falls after it escapes from the orifice. With an expiratory flutter valve mask one can get a higher concentration of oxygen than with the catheter, the nasal inhaler, or even a well run tent or chamber. At 4 liters a minute one can get from 29 to 33 per cent oxygen in the alveolar air of a tent, which was the same as a chamber giving from 35 to 39 per cent oxygen. At 6 liters we got from 35 to 42 per cent oxygen, which was the same as a chamber carrying from 39 to 40 per cent. With 8 liters we could get exactly as good oxygen concentration as in a chamber. The purpose of a tent is to confine oxygen, and when we confine the oxygen we also confine carbon dioxide, heat and moisture. We also stop or reduce the air circulation. It is thus necessary to provide an air conditioning adjunct to every tent. The great advantage of the chamber is that one can be with the patient. The great advantage of a tent is that there is nothing about the patient's face. The great advantage of the inhaler is that it can be applied to almost everybody, except those who are very sick or delirious and won't permit any device to stay

on the face, or patients with obstruction to their noses. Oxygen will never of itself, probably, cure a patient with pneumonia, but oxygen keeps the patient alive until his own mechanism or the serum brings about recovery.

I have encountered not infrequently commercial organizations that were selling oxygen equipment or providing rental service, who state that analyses have been shown to be unnecessary. That is absolutely untrue. Analyses should be made at frequent intervals. It is so simple that any really intelligent person in the home can be taught to carry it out. There is one thing ever to keep in mind in oxygen therapy, and that is the hazard of fire from explosion. It is practically negligible if precautions are observed. Keep sparks of any kind away from the vicinity of the oxygen equipment. It is not advisable to go into an oxygen tent with electrical equipment that is liable to make a spark. Inflammable materials that are more liable to spontaneous combustion should be removed.

Serum Therapy of Pneumococcic Pneumonia

DR. RUFUS I. COLE, New York: I have been able to study in the last few years more than 2,000 cases of pneumonia. Certain cases of pneumonia are associated with pneumococci in the sputum, certain other cases are associated with streptococci and others with staphylococci, but little thought has been given as to when pneumonia is actually present. The trouble is not so much to differentiate pneumonia from other conditions such as aneurysms or fluid but to say when a patient actually has pneumonia. In at least 60 per cent there occurs a preceding upper respiratory infection, and finally the patient begins to expectorate sputum and the doctor is called in.

Pneumonia is an acute inflammatory disease of the lungs. Sometimes pneumonia can be determined only by x-ray examination. My associates and I have had 1,600 and some cases which we call lobar pneumonia. We have had 200 cases of streptococcic pneumonia, a smaller number of staphylococcic pneumonia, and so on. But when all these cases are taken away, there is still left a group of cases in which pneumococci were present but the symptoms and features which we consider as characteristic of lobar pneumonia were not present. Those cases we call atypical pneumonia. The term "atypical pneumonia" is a better term than "bronchial pneumonia" for pneumonia in which the symptoms and signs are not characteristic. It is probably better, however, that every case manifesting severe symptoms, in which there is pain, cough and, above all, bloody expectoration, should be called lobar pneumonia and should be treated as such. The epidemic of pneumonia that occurred in 1917-1918 was undoubtedly due to streptococci. In 1918-1919 there was a great increase in staphylococci. It seems rather unimportant and rather misleading, therefore, to think of pneumonia as being a fixed condition. That is why it is so difficult to determine the exact therapeutic value of any kind of treatment. Not only does the kind of pneumonia vary, but the severity is of various grades. It is only a few years since all forms of intestinal infections were called inflammation of the bowels. This included typhoid, the paratyphoid fevers, dysenteries and formerly appendicitis. It seems to me that the situation with regard to pneumonia is similar. There are one or two conditions in which the features are characteristic and definite and in which the disease is probably transmissible directly from patient to patient. Then there is a group of conditions in which the symptoms are much less constant, which appear widely in a community and then may disappear entirely. It is interesting that, in all these atypical forms of pneumonia in which pneumococci have been found present, in no case have type I pneumococci been present and in a very limited number of cases type II. The question has sometimes arisen whether these type II infections were not due to the so-called II-a. When one talks, therefore, of the treatment of pneumonia, one has to talk of the treatment of a large group of conditions, and the treatment may be very different.

Many years ago it was thought that if patients with type I pneumonia could receive large amounts of serum and receive this serum intravenously so that it could reach the focus of infection, certain patients at least might be saved. This belief was based on experimental evidence, and it seems to me that even today this evidence is of great value in helping one to decide for oneself whether or not one will use this method in the treatment of type I pneumonia. Animals, and especially rabbits, could be actively immunized against very large doses of type I pneumococci. Finally, they could be given doses thousands of times larger than the dose which would kill an animal not so treated. Then we found that the serum of these animals, when placed in the peritoneal cavity of mice, together with doses of culture much more than would kill a normal mouse, resulted in the mice being entirely free from any symptoms. Other mice receiving smaller amounts succumbed readily. So we began the treatment of patients with large doses of immune serum received from horses. This serum was given intravenously. It required a little courage at that time to treat patients with these very large doses given intravenously; and if one is a little worried today about giving serum to patients in small doses, one may think how much greater our trepidation was when we gave 100 cc. of horse serum every few hours. But our experience soon showed that whereas many of these infected patients had previously had positive blood cultures, when the serum was given in large doses the blood cultures became sterile. That seemed to me more important than the fact that many patients recovered. Furthermore, the results so far as mortality statistics go have been most encouraging. Why we had to give such large doses of serum were at first obscure, but gradually it became evident, through laboratory studies, just why it was necessary. Pneumococci are virulent only because they possess capsules, and these capsules in some mysterious way prevent the leukocytes from taking them up and destroying them. There are various methods now for getting rid of these capsules. Pneumococci of the most virulent type may be made to grow having no capsules whatever, and these pneumococci when injected into animals cause no infection, and when they are placed in mixtures together with leukocytes the leukocytes take them up readily and destroy them. But this capsular substance is set free, as is now known, in the circulating blood and fluids of the body. In the very ill patient the amount of this capsular substance in the blood may be very large. It frequently is excreted in the urine. When immune serum is added to this capsular substance, the so-called antibodies of the serum become fixed by the capsular substance, and so the bacteria having capsules may be entirely unaffected by the immune serum. For instance, if one takes pneumococci, places them on a slide and adds a great deal of capsular substance to the surrounding medium, the amount of phagocytosis which occurs when the immune serum is added may be very slight. In the patient ill with pneumonia, before the pneumococci can be affected it is necessary that all the capsular substance in the body be attacked by sufficient serum so that there will be a surplus remaining after all the capsular substance has been united and fixed by the immune bodies. That is the reason why it is so important to give large amounts of serum. It is the reason why it is important to give the serum early in the disease, before large amounts of the capsular substance have been formed.

We have treated more than 500 cases of type I pneumonia with immune serum over a long period of years, and the results clinically have been uniformly satisfactory. In this series the mortality rate in the cases treated in the first three days has been under 4.8 per cent; in those treated on the fourth day it has been 8 per cent; on the fifth day, 8.6 per cent; on the sixth day, 19.5 per cent. It is therefore obvious that the earlier the patient is treated, the more satisfactory the results will be. Fortunately we have in New York State, I think, the best public health laboratory in this country and probably the best in the world. It has worked continually all these years on producing better serum—concentrating the serum. By that I mean removing the portions of the protein in the serum which are ineffective. As a result it has produced a serum which is concentrated at least three or four times. The methods of testing the serum have been greatly improved, although they are not ideal as yet, because no method of testing serum can be perfectly satisfactory in which living animals such as the mouse must be employed, which vary so much in their resistance and their susceptibility to disease. A method of deter-

mining the so-called immunity serum has been devised, so that we can tell with a considerable degree of accuracy just how much of the immune substance we are giving to patients. We have always given much more serum, I think, than any one else. Our dosage, when whole serum was employed, was 100 cc. at first, and we continued that every eight hours until there was definite evidence that the serum was effective. We have sometimes given over 2 liters of serum to a patient with lobar pneumonia, in a number of cases with good results. We now give 90,000 units at the first dose and repeat this as often as necessary until the symptoms are alleviated. I think this is very important. There is no way of telling accurately when a patient has had enough serum, but there is one method which helps us very much, and that has been a method devised by Dr. Francis. This method, however, is not completely accurate. In certain cases in which there is a positive skin reaction it has been necessary to give more serum. Large doses of serum should be employed and they should be repeated and continued until definite signs of effect on the course of the disease are obtained. We are fortunate in now having in this state a large supply of serum which we can feel is effective and trustworthy.

Up to recently, most of the serum used in the treatment of pneumonia was derived from horses. During the last year a number of cases have been treated with serum made by immunizing rabbits actively to pneumococci. The rabbit serum theoretically should be effective, chiefly because it has been shown that the molecular size of the protein which represents the antibody, when derived from the rabbit, is very much smaller than that in the horse serum. This has been determined by methods of ultrafiltration. The rabbit serum also has been much cheaper to make than the horse serum. Thirty-two cases have been treated with the rabbit serum, and the clinical results, so far as one can judge from mortality, have been very satisfactory. The objection to the use of the rabbit serum is that the chills, which occur also following the administration of horse serum, occur with greater frequency and severity when rabbit serum is employed. Various methods have been used to get rid of this chill producing substance. It has been found that by giving the patients acetylsalicylic acid just before the serum is administered the frequency and severity of the chills may be to a considerable extent reduced. We are now employing rabbit serum entirely with our patients, but I think this is a special problem, one that should be undertaken in a special place under favorable circumstances, until it can be determined whether or not rabbit serum is actually more effective than horse serum.

In some cases in our experience, where the fever continues high, where the respirations remain rapid, and cyanosis continues after two or three days of serum treatment, we have found a serious complication such as endocarditis or meningitis. In the last fifty-one cases of type I pneumonia treated with concentrated horse serum and rabbit serum, not one of our patients has died. This, however, is a record which probably cannot be repeated. I think all the statistics indicate that if serum is effective in type II pneumonia, it is much less effective than in type I. This would be expected from the experimental evidence. It is much more difficult to produce an effective serum for type II, and with such serum it is much more difficult to save animals highly infected. This was observed before we ever began treatment with serum, and the experimental evidence has been fully confirmed by clinical observation. However, some of the studies have indicated that the mortality rates in type II pneumonia may be reduced by the proper therapy and active use of type II serum. My own feeling is that every patient with type II pneumonia should receive serum; but the difficulties of treatment, the necessity for using large amounts of serum, the necessity for constantly observing patients, is greater when type II is present than in type I. Fortunately, in many communities the number of type II cases of pneumonia has decreased materially in the past few years. That is certainly true in New York City. I am told that in Rochester and in this district, however, a large percentage of patients with pneumonia suffer from this type of infection. In certain parts of the world, such as Scotland, 40 or 50 per cent of the cases of pneumonia are of type II. In New York, where previously we had as many as 35 per cent of the cases due to type II, there has been a distinct diminution. Last year we had only 11 per cent.

With regard to the other types in which serum is now provided—types V, VII, VIII and VI—these belong in the group in which the severity is much less. If we have a method by which the mortality may be reduced 3, 4 or 5 per cent, it certainly is justifiable and worth while to employ the serum when the diagnosis can be made. In these cases probably the importance of giving continued large doses is not so great as it is in the case of type I and II pneumonia. I would stress the fact that in type I pneumonia large doses must be given, they must be given often, and the doctor must see his patient frequently. When type II serum is employed, still greater attention must be given to the patient, larger doses must be given, and they must be given over a longer period.

The dangers of serum, I feel, have been to a certain extent exaggerated. After the administration of serum, in a few cases, there may be immediate reactions in the form of collapse, respiratory collapse, and so on. The number of cases in which these symptoms are of great severity, however, is very small. In my own experience I have seen only three or four cases of severe anaphylactic reaction. Most of the reactions can be promptly controlled by giving the patient epinephrine in small or large doses as necessary. Serum reactions that occur following the administration of serum occur in a considerable number of cases. These, however, are not serious. They are distressing to the patients, but the reactions which develop from forty minutes to an hour after the administration of serum are in most cases disturbing chiefly for the discomfort which they cause. The same may be said of the so-called serum disease. Patients complain a great deal about serum disease, and many patients say they would rather die of pneumonia than have serum disease. But when one compares the discomfort caused by this condition with the savings of life which occur from the proper administration of serum, it seems to me that serum sickness may be disregarded.

The chief points that I wanted to make in my talk are that the serum should be given very early, it should be given in large amounts, and its use should be continued as long as there is a chance of the serum affecting the outcome of the disease.

DISCUSSION

DR. ROGERS: Dr. Cole has made the point clearly as to why large amounts of serum are necessary; namely, that the circulating capsular substance in the blood stream must be neutralized by serum before it can get to the bacteria. It is equally important, therefore, to give the serum early, before large amounts of this excess substance get into circulation. Not only should it be given in large doses, but it has been definitely indicated by our experience in the last two years that it is necessary to complete within a relatively short time. Extensively spread dosage should be avoided. Dr. Cole mentioned the intradermal test devised by Dr. Francis, which, unfortunately, because of its difficulty of interpretation, is not a widely practical test. Dr. Bullowa has devised another test which is based on a temperature determination indicating the amount of circulating antiserum in the blood stream. We have accumulated data on almost 1,800 type I cases treated with serum. About 35 per cent of that represents experience in the homes, not in hospitals. There has been but one death that we are definitely obliged to stamp anaphylactic reaction. There have been a larger percentage, 7 or 8, of moderately severe reactions, but they have readily responded to appropriate treatment. If patients give a history of sensitivity a reaction may result. There are circumstances under which serum treatment is probably justifiable even though a reaction may be anticipated. The question of desensitizing is not academic, but serum can be given with great care. In relatively minor degrees of sensitivity epinephrine should help. To some degree there is another consideration which places the patient in the category in which treatment is justifiable, and that is pregnancy during the later months. That is distinctly a serious hazard. Dr. Cole mentioned the development of rabbit serum. My greatest fear is that if rabbit serum is used indiscriminately and reactions are encountered, it will perhaps darken the whole future of serum therapy. It should be a very real advance

when it has been perfected. There are at present a number of typing stations in the state. Type I serum is available in well over a hundred stations, and there are several providing type II. In the next few weeks we shall start distributing V, VII and VIII. We have, for instance, certain parts of the state where type V pneumonia is the major pneumonia, and there we shall provide type V serum. All are probably aware of the legislative appropriation for this purpose, which was made last spring. We did not get the money immediately, and it takes sometimes as much as a year to get a horse up to a point where his serum is satisfactory. As soon as possible, however, we shall provide our own serum. In the meantime we shall provide what we can and purchase the rest.

Pneumonia Clinic

DR. ROGERS: The clinic this afternoon is to be conducted by Dr. L. A. Kohn and Dr. W. W. Fray. Dr. Kohn will discuss the clinical side of the cases and Dr. Fray will discuss the roentgenologic phases.

DR. L. A. KOHN, Rochester, N. Y.: We are going to start off by showing a case of type I pneumonia.

Mr. P., a carpenter, aged 38, was admitted to the hospital on the third day of what proved to be type I pneumonia. His past history was irrelevant. He never had pneumonia before. He had a cold ten days to two weeks prior to October 5, when on returning home from his work on an outdoor job he noticed that he had a little pain in breathing. The next day, October 6, he went to work but that evening felt really sick. His temperature was 101.4 F. He had a cough and pain on both sides of his chest on breathing. The next morning there were no signs in his chest. His temperature was 104. He had a chill and began to produce rusty sputum.

The morning of the third day of the disease, the day of admission to the hospital, the temperature was still higher, he raised more rusty sputum, and the physician found definite signs of pneumonia. On his arrivel at the hospital his sputum was taken in the emergency ward and sent to the laboratory and found to contain the type I pneumococcus. His temperature was over 105, the pulse was rapid, 120, and the respirations were rapid. The blood pressure was 110 systolic, 60 diastolic. He was slightly cyanotic, he was perspiring, his breathing was rapid and shallow. He was slightly jaundiced. There was physical evidence of a well developed pneumonia in the lower part of the right lung in back.

The white blood count was 31,000. Blood chemical studies revealed that the nonprotein nitrogen was 59. There was slight jaundice in the blood serum. The icterus index was 18. The blood chlorides were reduced to 517 as opposed to a normal of somewhere around 590. The urine was typical of the febrile patient.

Prior to giving serum, a blood culture was taken, and a careful history was taken to obtain evidences of allergy, or previous experience with serums. The cutaneous test was done and the ophthalmologic test was done, and as both were negative, 50,000 units of type I serum was given the patient that evening, diluted to about 100 cc. with sterile salt solution. Prior to this large dose, 1 cc. was given very slowly, diluted to 10 cc. by sterile salt solution and an interval was allowed to elapse before he was given the full initial therapeutic dose. There was no reaction to the small dose, but forty-five minutes after the dose of 50,000 units he had a chill and his temperature rose to 106.2. He was given a tepid sponge bath, his temperature dropped, and about four hours later he was given another 50,000 units. There was no reaction to the second dose.

The next day he received an additional 100,000 units. That made 200,000 within the first four days of the disease. His temperature had fallen not to normal but appreciably, without a critical sweat within the next twenty-four hours, and as the blood culture had failed to show growth it was decided to give him no more serum.

By the sixth day of the illness there were distinct evidences of resolution in the right lower lung. The breathing was not so rapid, and the general condition was improved. On the seventh day of the illness the white blood count dropped to 10,000, and with minor fluctuations it has remained normal.

This is the fourteenth day of the disease. In his chest at this time there are still a few coarse râles, but most of the dulness and I think all of the abnormal breath sounds have disappeared. He is still coughing a little.

[Here and at other points during Dr. Kohn's talk, Dr. W. W. Fray, Rochester, N. Y., showed slides of the roentgenograms of the chest of the patient, describing evidences of the disease as shown in the roentgenograms.]

People who attended or examined this patient wore a mask and washed their hands when they left. We consider that all cases of pneumonia are communicable and that people should be protected from possible contagion. The patient was given an adequate amount of fluid and as much food as he could eat without causing further distention. He was given 6 Gm. (90 grains) of sodium chloride in the form of pills daily, in addition to salt in his food. He was given mild sedatives to control his cough, and once or twice a small dose of morphine.

One topic that Dr. Fray and I were asked to discuss was that of complications of lobar pneumonia. Of the serious complications of lobar pneumonia, or of pneumonia in general, the only one which can be distinctly influenced is empyema. There is only one sure way in the long run of diagnosing empyema, and that is to find pus with a needle. Conversely, if one wants to be sure that there is no pus, it is only the needle that will settle the question. As far as I know, no patient has been permanently hurt by having a needle put in the chest when there was no pus there. On the other hand, failure to put a needle in the lung may make a serious difference to the patient. When a patient has a persistent elevation of temperature, persistent elevation of white count, persistent elevation of pulse or any one of these, empyema must be suspected, whether or not there are physical signs.

Meeting of the Medical Society of the County of Monroe, New York

DR. E. G. WHIPPLE, Rochester, N. Y.: About two years ago the Medical Society of the State of New York, the State Department of Health, and associated with them the Metropolitan Life Insurance Company started an attempt in New York State to lessen the morbidity and mortality from pneumonia. This central group asked each county society to form a local committee. Our local committee has attempted two things. One was to see that information is constantly kept before the medical profession and that such information as is deemed advisable is given to the public.

It is my pleasure and privilege to present Dr. Jesse G. M. Bullowa of New York, clinical professor of medicine at New York University and visiting physician at Harlem Hospital.

The Management of the Pneumonias

DR. JESSE G. M. BULLOWA, New York: I shall give especial emphasis to the specific treatment of the pneumonias with the various serums that are available, to the diagnosis of pneumonia, and to some of the complications.

Most of the primary pneumonias of adults, probably 85 per cent, are due to pneumococci. Probably half of the primary pneumonias of children are due to pneumococci. It should not be forgotten, however, that some of the secondary pneumonias —the pneumonias of children ill with the infectious diseases— are due to pneumococci. Probably one in eight or ten children who develop pneumonia after measles or pertussis has a pneumococcic pneumonia. At the Willard Parker Hospital we had a child with pertussis pneumonia. We found that he had pneumococcic pneumonia, type V; he received serum and recovered. We have had many similar cases. We must make the diagnosis of pneumonia on the clinical evidences, on the history, and on presumptive signs. In pneumonia a history of a common cold which has lasted one or more days precedes the chill or pain in the side of the chest in about 70 per cent of the cases. Then there is a cough—a cough which may or may not be productive.

The diagnosis of pneumonia is often a very simple matter, but often enough it is a matter which requires considerable skill and every possible laboratory aid, including x-ray examinations, blood cultures and other examinations to eliminate other conditions. About one fourth of the cases of coronary occlusion that come to Harlem Hospital come first to my service, because a diagnosis of pneumonia has been made.

I hope that the day will come when the diagnosis of pneumonia will be qualified by its etiologic agent, obtained either ante mortem or, if necessary, post mortem; and when that day comes, the physician will have to explain pneumonia deaths just the same as operative deaths.

The whole diagnosis of the type of the pneumococcus which is involved in a pneumococcic pneumonia depends on the capsule swelling—the swelling of the capsule when the organism is brought into contact with specific antiserum. At Harlem Hospital we have abandoned all other methods of typing pneumococci, not because they are difficult to do or because we have not believed in them, because we developed the slide agglutination test in our laboratories, but because we find them no longer necessary. We do a direct sputum examination or examination of the discharges that contain pneumococci. It may not be feasible to spend a sufficient amount of time searching large quantities of sputum for a single pneumococcus, so that we always employ where necessary the mouse inoculation method. The peritoneum of the mouse is a selective culture medium for pneumococci. Not only do the pneumococci grow there and the other organisms die off or are inhibited; the pneumococci in the blood stream of the mouse cause a septicemia.

There are about thirty-two different types of pneumococci. When a report is received that the organism does not belong in any of the types, or when it is type IV (unless it is IV Hooper) or group X, doubt should temporarily be cast on such a report, because the chances are overwhelmingly great that another specimen or more careful study of the same specimen will reveal a pneumococcus of definite type. In 1928-1929 we had 34 per cent of our cases that were not typed. In 1933-1934 we had only six cases, or 1.2 per cent of the cases that were studied at Harlem Hospital in adult patients, and about the same number of children, that were not typed. That experience has lasted from 1934-1935, 1935-1936 and 1936-1937, so that I think that it can be said with some definiteness that practically 98 per cent of the pneumococcic pneumonias are due, at least in our community, to pneumococci of specific type for which a typing serum is available. It is true that there are a few additional types which have been recognized, and some of them have been given numbers and some may be substituted for other numbers, like XXVI, a type which is now in dispute, and also XXX. But most patients will suffer from pneumococci which can be given a number.

There is quite a difference in the prognosis in the different types, not only in the prognosis; there is also a great difference in the treatment, because pneumococcus type I pneumonia is benefited by pneumococcus type I serum, and pneumococcus type II pneumonia is benefited only by serum which is appropriate to that type. Pneumococcus type I invades the blood stream in about one fourth of the cases, while pneumococcus type II invades the blood stream more frequently. In the bacteremic cases of the various types the death rate is almost always high, whereas in the nonbacteremic cases it is almost always low. That demonstrates the importance of knowing not only the type of case that is involved but also whether there is a bacteremia or not. It has been my experience that the blood stream is invaded usually in pneumonia of types I and II on the fourth day or later, and it may be invaded quite late in the disease.

Every year we have probably twenty cases admitted to the tuberculosis service at our hospital which are subsequently transferred to us as cases of pneumonia. We have cases that are admitted to us as pneumonia that we transfer to tuberculosis. Sometimes we have both organisms present.

A fall in the pulse rate is the most important single point in judging whether one has given enough serum. Giving too little serum is wasteful of life and of serum, because, unless the patient's life is saved, all the serum given is wasted. Serum treatment should not be judged by whether a patient has received serum or not. A patient who does not receive a very intense, very concentrated, ample amount of serum—a sufficient amount so that all the organisms are sensitized and can be engulfed by leukocytes—cannot get well.

I want to emphasize the inaccuracy of the common statement in the literature that serum does good only in the first three days of the disease.

It takes time to treat a patient with pneumonia. It may take six or eight hours, but then treatment is done, as a rule, and the rest of the treatment is relatively simple.

One objection to serum has been that it is expensive, but that is a very specious objection. The average cost of serum for a patient with pneumococcus type I pneumonia is probably $35. The longer one waits, the more it is going to cost, and the longer one hesitates about giving serum the longer the illness is going to be, the more money will have to be spent for hospital days care or for special nurses, and one may not have the patient in the end.

The most common type in most communities is pneumococcus I. Next in order are types III, II, VIII, V and VII. We have good serums for types I, II, VIII, V, VII, XIV, IX, XVIII, VI, XIX and XII. We also have a serum for type XVII. We had a serum for type XX but it is exhausted, but we shall have another supply. If we confined ourselves only to the four most prevalent types for which we have serums, we would be able to treat 70 per cent of the pneumococcic pneumonias encountered.

I want to emphasize again that one cannot compare pneumonias as a group; one must compare them only as types.

We had fifty-four patients who were treated with serum in the first four days, and the mortality was 20 per cent. Sixteen patients treated were bacteremic, and only seven of these died, or a mortality of a little over 40 per cent. The ratio of the difference between the serum and the non-serum cases is 2.6. Now 2.6, when comparable populations are compared and the total numbers included are over 30, means that there are about 970 chances out of 1,000 that there is a significant difference and that the difference in the results is due to the difference in the populations. When we took the first four days serum treatment and compared it with the sixty-two cases treated on the fifth day or later, we found that the ratio of the difference to the error in the early treated cases to the late treated cases is 2.2. It is frequently said that treatment of pneumococcus type II pneumonia is of doubtful value, but I think that after this demonstration, it cannot be said of cases treated before the fifth day. Pneumococcus type II pneumonia requires a great deal more intensive treatment than other types. It requires probably twice as much serum. It requires early treatment.

Of 133 patients with type I pneumonia treated in the first four days, 6 per cent died; sixteen patients were bacteremic and 18 per cent died. After five days there were 190 patients, with 8.9 per cent deaths; there were thirty-four bacteremic patients, with 29 per cent deaths. The ratio of the difference to the error is 1.5, which is not significant. It is never too late to give serum.

With proper precautions, the incidence of anaphylactic deaths from serum is about one in 500. Without serum, in pneumococcus type I pneumonia the death rate is one in five. Good refined serum is less apt to give a reaction than crude serum. A good history should be taken. A test for sensitivity should be used—the ophthalmic test or the intradermal test. And it is very important to wait at least twenty minutes before reading the results. For rabbit serum we use an intravenous test. We inject very slowly 0.1 cc. of the rabbit serum diluted with 10 or 20 cc. of saline solution, and if there is no fall of blood pressure, or not more than 20 mm., we do not hesitate to go ahead and give the serum. I do not believe that one can desensitize a patient if the patient is sensitive to serum, but that does not mean that the patient should not get serum. If one doesn't give serum one may lose the patient anyhow. I do believe one can give serum by inducing a refractory state by giving epinephrine, 5 cc., and then waiting at least eight minutes and then slowly injecting the serum. We inject it into the tube of an infusion set and while the patient is in an anaphylactic state.

I should like to mention briefly the adjuvants in the treatment of these pneumonias. I have already mentioned oxygen in my talk at the Pneumonia Institute. If the patient cannot be relieved of his anoxemia, he may not survive to be cured by the serum. Another thing is food. We give our patients a full diet during pneumonias. One never can tell how long a patient with pneumonia will last. He may have more hours of elevated temperature than a patient with typhoid. Another very important thing is the retention of tissue turgor. We

find that the giving of salt, the giving of infusions to prevent dehydration, the prevention of salt loss, or its replacement if there has been a salt loss, are of vital importance. The best way is to give a 10 per cent solution of sodium chloride, perhaps 30 or 60 cc., and restore the salt without increasing the heat. Few of our patients die as the result of dehydration, and there are a few who die of pulmonary edema. Those are the two main causes of death.

How do we treat pulmonary edema? There are several things. First, we want to extract from the lung as much fluid as possible into the circulation, and we do that by injecting 50 per cent sucrose solution, which stays in the circulation for a longer time than dextrose. We use 100 cc., and we may have to repeat that amount. Another thing that happens in pulmonary edema is that the antrums leading into the alveoli may be filled with bubbles of fluid, which keeps the oxygen away from the blood capillaries. We feel pretty certain that we can break through these capillaries by giving the oxygen in a pressure of 10 mm. of water. We do that with a closed system of oxygen and use a rapid flow of oxygen, probably 15 cc., and measure the amount of pressure in a manometer.

DISCUSSION

DR. WILLIAM S. MCCANN, Rochester, N. Y.: The thing that impressed me most was the way in which Dr. Bullowa follows through—checking up on the adequacy of serum administration. When he had evidence of the adequate administration of a certain type specific serum, and still something seemed to be going wrong with the patient, he investigated the possibility that other types of pneumococci were involved. The whole system by which he has checked himself up is most impressive. I think every one is grateful to him for the point on the importance of the dropping pulse. One thing I missed was a discussion with regard to the frequency and the circumstances under which aspiration from the lung is used.

DR. D. B. JEWETT, Rochester, N. Y.: I think I must belong to that era previous to 1934. We analyzed our pneumonia cases in the Genesee Hospital within the last year, and our mortality for all type I cases, 150 or 160 cases, was 16 per cent. That is a pretty bad mortality compared with a mortality of 2 or 3 or 5 per cent. I think the secret is that we haven't used serum in adequate amounts and at frequent enough intervals. I presume our percentage of 16 is rather general, but it is obvious that it is not at all the ideal rate.

DR. G. P. BERRY, Rochester, N. Y.: It seems to me that pneumonia is as much a hospital problem as diabetes. It requires continual following of the patient, laboratory studies, continuous service in the ward. The first hours are the important ones.

DR. P. H. GARVEY, Rochester, N. Y.: I think Dr. McCann asked Dr. Bullowa the one point I was interested in. We have difficulty in a number of cases in getting sputum early or getting positive blood cultures early. I wonder how long they wait before they do a lung puncture on a patient to obtain positive evidence of a specific type.

DR. E. B. SOBLE, Rochester, N. Y.: I want to ask whether Dr. Bullowa at the Harlem Hospital ever does a urine typing any more. Sometimes we used to have to do that when we couldn't get sputum and before we tried taking lung punctures.

DR. P. W. BEAVEN, Rochester, N. Y.: Referring to the use of rabbit serum, how much rabbit serum is displacing horse serum as a means of treatment?

DR. B. J. SLATER, Rochester, N. Y.: Would it be possible in this city, in the various hospitals, to set up certain standard procedures which should be followed in all cases of pneumonia, for example, taking blood cultures, so that when a patient is brought into a hospital he would be assured that he would come under the advantage of a system such as Dr. Bullowa has in New York? Dr. Bullowa's lecture was very illuminating and enlightening to me.

DR. JOSEPH ROBY, Rochester, N. Y.: I should like to ask Dr. Bullowa a question: If one can get the same amount of concentrated serum that we used to give of the old serum, I am wondering about giving 125,000 units at the first dose. Does Dr. Bullowa think that that would be a more dangerous procedure than giving it every two hours? I will confess that I am much more familiar with the old serum and perhaps have no right to ask that question.

DR. E. G. WHIPPLE, Rochester, N. Y.: Dr. Bullowa, will you kindly close the discussion?

DR. J. G. M. BULLOWA, New York: We did about 2,500 lung suctions at the Harlem Hospital. I have published the mortalities in my recently published "Management of Pneumonias." We did that, of course, to determine the reliability of the typed sputum. We know that in 7 per cent of the cases the type obtained from the sputum may not be the type actually causing the disease. In skilful hands—and I train my interns to do it skilfully—we have seen no harm come from it. We have sometimes seen harm come from it in the hands of an intern who was not well trained. Occasionally, if we do it late in the disease, we get a dislodgment of an embolus. Occasionally we get some bleeding, and that may do harm. The thing should be done quickly. If one dallies over it, one is bound to have the patient breathe, and then the needle will cut the lung. It is not necessary in every case. One can turn the patient on his side with the involved side uppermost, have him stay there a short time, and secretion will usually come down into the bronchus and be coughed up. It may not be much sputum, but a tiny fleck can be obtained. As a routine we use laryngoscopy, making the patient cough, having the patient cough against a swab, and thus collecting a tiny fleck of mucus. Then we incubate the swab in broth for three hours and then inject the broth into a mouse. We don't use urine typing. If there is sufficient antibody in the urine, the patient is terribly ill and one can probably get it out of the sputum or blood. Testing urine is not easy. Only about 10 per cent of the series showed a positive urine. Those were very sick patients and it was not necessary to use that method.

Dr. Beaven asked about rabbit serum. Nobody can tell whether rabbit serum will displace horse serum. The reasons for trying rabbit serum are, first, patients may be sensitive to horse serum; secondly, it is probable that the rabbit serum does, as Goodrich suggests, penetrate farther than horse serum. There are also commercial reasons—it requires a much smaller investment of capital.

Those of us who are working with horse serum will have to work with the manufacturers until they can produce a serum which is concentrated, which should have about 4,000 to 5,000 units per cubic centimeter, which should be possible to give in large doses without giving acetylsalicylic acid first. With the processed rabbit serums we have given about 200 cc. and even more at a single injection, preceding the injection with acetylsalicylic acid so as to have the patient in a refractory state. The reason we do not give the horse serum in a large single dose, which is the ideal way, is that we think the chill is distinctly harmful. We do not like to give serum to a patient who has a high temperature, so we frequently lower these high temperatures first so as to have a margin of safety. When the temperature is down to 102, we continue to give the serum. The reactions usually come about one hour or an hour and a half after the injection, so we set the two hour interval so that if there is a reaction we shall not give additional serum. Why some serums can be given in doses of 2 cc. or 10, 25 or even 40, without the chill, and others cause a chill with 0.5 cc. I don't know. It is that problem with which we are most concerned at the present time—to get a serum that won't give a chill when given in a dose of 125,000 or 200,000 units. We want to be able to give it without giving acetylsalicylic acid.

Answering the question Dr. Slater raised about standard procedure, one of the most difficult things about my pneumonia service is the preservation of the skills that I require. When I lose my interns I have to start all over again. That is probably one of the troubles in most hospitals. Unless there is one man who can plan for a long time in running a pneumonia service—I have planned sometimes for two or three years ahead how I am going to get serum and other things for my service, and then I have to educate my interns—unless there is one man in each place who will preserve the skills and keep the interns instructed, one will find it difficult to duplicate what we have been doing in New York. Unless each man is willing himself to plan ahead, it would be very difficult to acquire these skills and train the interns.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. HOWARD A. CARTER, Secretary.

SUPER FISCHERTHERM (6 METER) ACCEPTABLE

Manufacturer: The Fischer Corporation, 673 Ivy Street, Glendale, Calif.

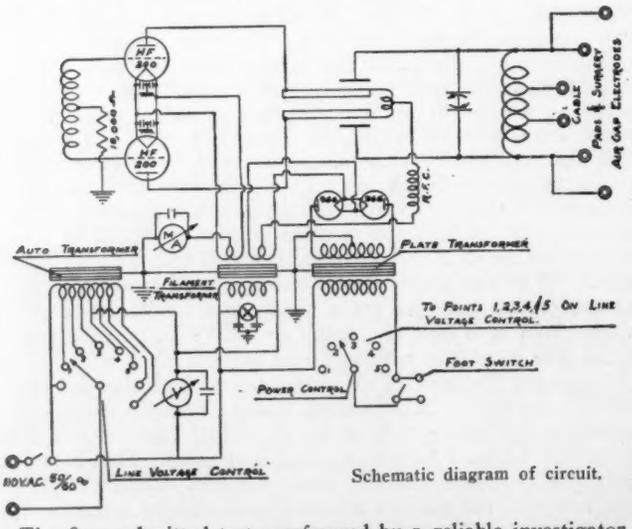
The Super Fischertherm Short Wave Diathermy Unit (Model 114-A) is recommended for medical and surgical use in the office or the hospital. It is housed in a walnut cabinet with vertical bakelite panel; there are aluminum ventilators in the top and back and wood ones in the sides. The chassis is of pressed steel. The subpanel is of wood with a galvanized iron shield on the lower side; high frequency insulation is porcelain, including tube sockets and coil supports. A large drawer occupies the lower part of the cabinet. The unit weighs approximately 180 pounds and is 39½ inches high by 31½ inches wide by 21½ inches deep. Standard equipment includes inductance cable, cuff and pad electrodes and surgical accessories for coagulation, desiccation and cutting purposes. Air spaced electrodes and supporting arms are optional.

Super Fischertherm (Model 114-A).

The circuit consists of two vacuum power tubes and two rectifier tubes in a simple arrangement. The output circuit is tuned by a split stator condenser. In adjusting for line voltage, an ohmite tap switch and a variable condenser resonance control are used.

The power input is approximately 1,300 watts. Since no reliable method for determining output power has been established, this value is not stated. The transformer temperature rise and the temperature rise at different levels within the cabinet were within the limits of safety prescribed by the Council. Burns may occur with this unit but are less likely than with conventional diathermy and may be avoided by the use of ordinary precautions.

A filter to prevent feed-back of radio frequency current into the power line is included in the equipment.



Schematic diagram of circuit.

The firm submitted tests performed by a reliable investigator with regard to the heating ability of the unit when applied to the living human thigh. Eight tests were made with each of these technics: air spaced disks, cuffs and inductance cable. Four healthy male medical students were used for the observations. Experiments were conducted on the left and right thighs alternately. Temperature measurements were made with thermocouples inserted into the anterior portion of the thigh at depths of one-eighth inch, three-fourths inch and 2 inches or on the bone as measured from the skin straight in. The averages for the eight observations with each technic are given as follows:

Averages of eight observations, air-spaced disks:

	Deep Muscle	Subcutaneous	Skin	Oral
Initial	100.2	99.2	96.0	98.8
Final	101.4	101.5	98.0	99.1

Averages of eight observations, cuff technic:

	Deep Muscle	Subcutaneous	Skin	Oral
Initial	99.5	98.3	93.7	98.7
Final	102.8	103.3	100.3	99.1

Averages of eight observations, inductance cable technic:

	Deep Muscle	Subcutaneous	Skin	Oral
Initial	99.6	98.6	93.7	98.7
Final	101.8	103.4	100.1	99.0

In applying the inductive cable, approximately 1 inch of bath-toweling was wrapped round the thigh and it was held in place by approximately four wraps of inductive cable. The position of the air-spaced electrodes was measured from the surface of the pads to the patient, from 2¼ to 3 inches. In addition to the spacing there is from one-sixteenth to one-eighth inch of rubber covering on the disk. The spacing of the two electrodes was made the same. The resulting temperature rises are higher than those achieved with a conventional diathermy tested at the same time.

The unit was tried out in a clinic acceptable to the Council and performed satisfactorily.

In view of the foregoing report, the Council voted to include the Super Fischertherm in its list of accepted devices.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. PAUL NICHOLAS LEECH, Secretary.

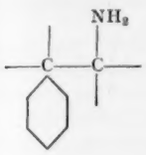
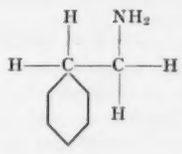
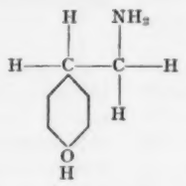
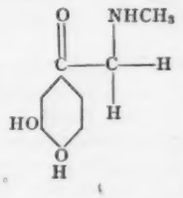
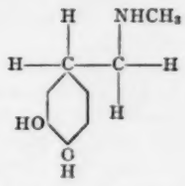
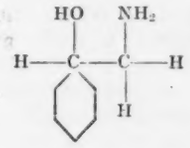
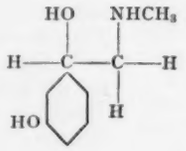
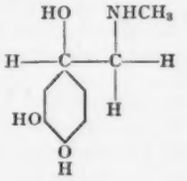
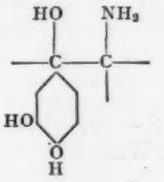
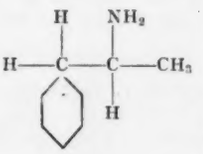
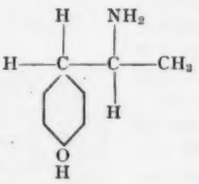
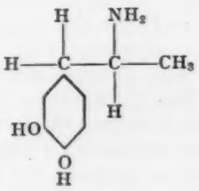
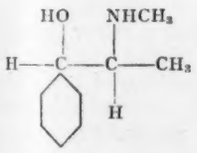
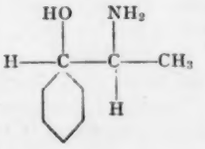
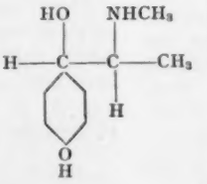
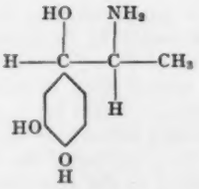
PRESENT STATUS OF BENZEDRINE SULFATE

The manufacturers of Benzedrine (Smith, Kline and French) have presented Benzedrine Sulfate and propose its use in various pathologic and substandard conditions of the central nervous system. Benzedrine, which stands accepted for New and Non-official Remedies, is the base, which readily changes to the carbonate on exposure to air (both are volatile) and is used by inhalation, whereas the sulfate is given orally. Review of the older as well as the newer pharmacologic and clinical data was required because of the great variety of conditions in which the sulfate was claimed to be useful.

EARLY PHARMACOLOGY

The experimental work with this drug consisted for the most part of the studies of the closely related phenylethanolamine (benzedrine is beta phenylisopropylamine) (see accompanying chart) and consideration must be given to this work. Alles [1] noted that Barger and Dale [2] had concluded that "the optimum carbon skeleton for sympathomimetic activity consists of a benzene ring with a side chain of two carbon atoms, the terminal one bearing the amino group" and that "another optimum condition is the presence of two phenolic hydroxyls in the 3, 4 position relative to the side chain; when these are present an alcohol hydroxyl still further intensifies the activity"; that Chen and Meek [3] found that tyramine and ephedrine had closely comparable physiologic activity, and that the work of Tainter

1. Alles, G. A.: The Comparative Physiological Action of Phenylethanolamine, J. Pharmacol. & Exper. Therap. **32**: 121 (Dec.) 1927.
2. Barger, G., and Dale, H. H.: J. Physiol. **51**: 19, 1910.
3. Chen, K. K., and Meek, W. J.: A Comparative Study of Ephedrine, Tyramine and Epinephrine with Special Reference to the Circulation, J. Pharmacol. & Exper. Therap. **28**: 59 (July) 1926.

Phenylamino-	Phenylamino-	Hydroxyphenylamino-	Dihydroxyphenylamino-		
					ETHANE
Primary configuration from Barger and Dale description	PHENYLETHYLAMINE α-phenyl β-amino ethane	TYRAMINE 4-hydroxy α-phenyl β-amino ethane	KEPHRINE 3,4-dihydroxy α-phenyl β-methylamino α-keto ethane	EPININE 3,4-dihydroxy α-phenyl β-methylamino ethane	
					ETHANOL
	PHENYLETHANOL-AMINE α-phenyl β-amino ethanol	NEOSYNEPHRIN 3-hydroxy α-phenyl β-methylamino ethanol	EPINEPHRINE 3,4-dihydroxy α-phenyl β-methylamino ethanol	Secondary configuration from Barger and Dale description	
					PROPANE
	BENZEDRINE α-phenyl β-amino propane	4-hydroxy α-phenyl β-amino propane	3,4-dihydroxy α-phenyl β-amino propane		
					PROPANOL
EPHEDRINE α-phenyl β-methylamino propanol	PROPADRINE (nor-Ephedrine) α-phenyl β-amino propanol	SUPRIFEN 4-hydroxy α-phenyl β-methylamino propanol	COBEFRIN 3,4-dihydroxy α-phenyl β-amino propanol		

BENZEDRINE AND RELATED COMPOUNDS

NOTE.—This chart indicates the chemical but not the stereochemical relationship of these compounds. *Kephrine* is included with the ethanes, from which it differs only in that an oxygen replaces two hydrogens on the α carbon. A correct chemical name for the compound is 3,4-dihydroxy benzoyl methylamino methane. *Synephrin* is not included but differs from Neosynephrin in having the phenolic hydroxy in the 4 instead of in the 3 position. *Benzedrine, Ephedrine, Epinephrine, Kephrine, Neosynephrin* and *Propadrine* are Council accepted either in the form of the base and/or of a salt of the base.

and Chang [4] and of De Eds and Butt [5] indicated that tyramine and ephedrine raise the blood pressure by a different mechanism than that of epinephrine.

Alles [1] studied the structure of ephedrine on the basis of the Barger and Dale [2] configuration and the work of Schultz [6] and Tiffeneau.[7] He noted that it would be deduced that ephedrine would be less active than phenylethylamine but that actually the latter is considered to have one-fifth the activity of tyramine, which in turn is considered to be equivalent to ephedrine in circulatory effect. He believed that the discrepancy was at least partially due to the differences in the drug's initial and final effects as demonstrated by Chen.[8] Alles [1] then undertook his study of phenylethanolamine.[9] He found that it had a greater blood pressure effect in rabbits than phenylethylamine (initial effect greater and final effect comparable, resembling

4. Tainter, M. L., and Chang, D. K.: The Antagonism of the Pressor Action of Tyramine by Cocaine, J. Pharmacol. & Exper. Therap. **30:** 193 (Jan.) 1927.
5. De Eds, F., and Butt, E. M.: Further Evidences of the Nonsympathomimetic Action of Ephedrine, Proc. Soc. Exper. Biol. & Med. **24:** 800 (May) 1927.
6. Schultz, W. H.: Bull. 55, Hyg. Lab., U. S. P. H. S., 1909.
7. Tiffeneau, W., quoted from Guggenheim: The Biogene Amine, ed. 2, p. 310.
8. Chen, K. K.: A Comparative Study of Ephedrine, Pseudo-Ephedrine and β-Phenyl-Ethylamine, Arch. Int. Med. **39:** 404 (March) 1927.
9. Phenyl-B-Amino-Ethanol First Prepared by Mannish, C., and Thiele, E.: Arch. Pharm. **153:** 181, 1915.

first epinephrine and then ephedrine), while its toxicity (subcutaneously in guinea-pigs) was found to be one-third that of ephedrine and one-fourth that of beta-phenylethanolamine. Tainter[10] also studied the pharmacology of phenylethanolamine and concluded that it resembled tyramine and ephedrine more than epinephrine.

Miller and Piness[11] studied phenylethanolamine sulfate and concluded that it was comparable to ephedrine pharmacologically and was considerably less toxic. It was found to be inactive orally and to have an advantageously weak pressor effect but a disappointingly weak bronchodilator effect on injection.

Later Piness, Miller and Alles[12] studied the three related compounds—phenylethylamine, phenylmethylamine and phenolisopropylamine (benzedrine). Testing the substances on dogs, they found the latter to be the only one which caused a marked rise in blood pressure which lasted for over three hours.

Tainter[13] believed that benzedrine would eventually prove superior to epinephrine and ephedrine and it is interesting to note that even at this time Alles[14] pointed out that Tainter and Hanzlik (unpublished) had completed some work that indicated that the action of these compounds was more complicated than previously suspected.

Four isomeric phenylpropylamines were studied by Hartung and Munch[15] in their series on amino alcohols. They noted that Chen, Wu and Henriksen[16] and Piness, Miller and Alles[12] attributed the oral efficacy of ephedrine to the presence of the third carbon on the side chain and in accordance found the phenylpropanolamine was active by mouth, whereas phenylethanolamine was not. They concluded that the optimum skeleton for pressor compounds was beta-phenylethylamine; that a shift in the relative position of the phenyl and amino groups very greatly decreases pressor activity; that substitution of a methyl on either of the two carbons in the side chain of this skeleton confers oral activity, and that the presence of the secondary alcoholic hydroxyl in phenylpropylamine serves to decrease the toxicity to a degree that becomes significant therapeutically.

Tainter[17] believed that the optimum configuration of molecules for pressor activity consists of the location of the amino and phenyl groups on adjacent carbon atoms and that the phenyl group must be on a terminal carbon. It is apparent that there is general agreement on the configuration which results in the pressor effects when these chemicals, including Benzedrine Sulfate, are administered orally.

RHINOLOGY

Miller and Piness[11] suggested that the greatest usefulness of phenylethanolamine would be in topical application to the nose. In the same issue of THE JOURNAL the Council published a brief statement[18] noting that confirmatory reports were necessary before acceptance would be in order. Piness, Miller and Alles[12] tested it and benzedrine by mouth and subcutaneously in animals. They attributed the duration of the effect as well as the oral effect to the side chain methyl group.

Bertolet[19] found benzedrine useful in 122 cases of nasal congestion. He did not refer to the previous work of Hartung and Munch[15] and Piness, Miller and Alles.[12] However, neither of them had used this drug by inhalation, and Bertolet appears to have been the first to use it in this manner. It was supplied to him in a suitable device by the manufacturer. He considered it an advantageous addition to rhinologic materia medica because it was safe, portable and an effective measure for use between office treatments. He believed that the contraindications were negligible but that it should be used only as prescribed by, and under the direction of, the physician.

COUNCIL ACCEPTANCE

At this time the Council declared benzedrine accepted for inclusion in New and Nonofficial Remedies[20] as a vasoconstrictor for local application and inhalation in rhinology.

Following the publication of the Council report, Byrne[21] reported the use of benzedrine in the treatment of fifty-one cases of various types of rhinitis. In the vasomotor type he found that the amount of secretion was diminished, the itching and feeling of fulness relieved and decongestion accomplished. His results in cases of sinusitis were poor—the drug even aggravated the condition in some cases. He felt that care should be taken in prescribing it.

Wood[22] used the drug in the treatment of diseases of the eustachian tube and the middle ear. He attached a pressure line and a nasal catheter to the benzedrine inhaler and described the advantage of vapor over liquids used in a similar manner for the treatment of these conditions.

Scarano[23] compared the rapidity of shrinkage and reactions following local application of ephedrine and benzedrine. He encountered no appreciable difference in shrinking effect and did not encounter burning, lacrimation and sneezing nearly as much with benzedrine as with ephedrine. Secondary reactions such as returgescence, atony and bogginess were less severe and less frequent with benzedrine. The drug has enjoyed widespread use and seems to be an effective, convenient agent for the purposes for which it was accepted, provided precautions are taken to avoid overdosage as recommended in New and Nonofficial Remedies and on the labels.

BENZEDRINE SULFATE

The sulfate, however, is recommended for oral use in a variety of clinical conditions. The Council is fully aware of the widespread publicity which has followed in the wake of the launching of this new form of benzedrine. Attention was called to certain abuses editorially in THE JOURNAL[24] as well as in the *British Medical Journal*[25] and the *Pharmaceutical Journal*.[26] Apparently the firm has some qualms about the rather extensive use of the drug and has mailed to many physicians a letter which suggested some caution in its use.

The extensiveness of the claimed uses in this letter, as well as those suggested in the lay press, demands a rather thorough consideration of the pharmacologic and clinical studies which have been reported since the Council acceptance of benzedrine. The A. M. A. Chemical Laboratory has examined this brand of benzedrine sulfate and found it to be satisfactory.

LATER PHARMACOLOGY

The pharmacology of phenylisopropylamine was studied rather extensively by Detrick, Millikan, Modern and Thienes.[27] They mentioned the early work of Hartung and Munch[15] and noted that Pedden, Tainter and Cameron[28] and Cameron and Tainter[29] confirmed the actions of this drug on dogs as

10. Tainter, M. L.: The Pharmacological Actions of Phenylethanolamine, Proc. Soc. Exper. Biol. & Med. **25:** 275 (Jan.) 1928.
11. Miller, Hyman, and Piness, George: A Synthetic Substitute for Ephedrine, J. A. M. A. **91:** 1033 (Oct. 6) 1928.
12. Piness, George; Miller, Hyman, and Alles, G. A.: Clinical Observations on Phenylaminoethanol Sulfate, J. A. M. A. **94:** 790 (March 15) 1930.
13. Tainter, M. L., in discussion on Piness, Miller and Alles.[12]
14. Alles, G. A., in discussion on Piness, Miller and Alles.[12]
15. Hartung, W. H., and Munch, J. C.: Amino Alcohols: VI. The Preparation and Pharmacodynamic Activity of Four Isomeric Phenylpropylamines, J. Am. Chem. Soc. **53:** 1875, 1931.
16. Chen, K. K.; Wu, C. K., and Henriksen, E.: Relationship Between Pharmacological Action and Chemical Constitution and Configuration of Optical Isomers of Ephedrine Related Compounds, J. Pharmacol. & Exper. Therap. **36:** 363 (July) 1929.
17. Tainter, M. L.: Comparative Actions of Sympathomimetic Compounds: Phenyl and Substituted Phenyl Derivatives, Non-Phenylic Ring Compounds, and Aliphatic Amines, Arch. internat. de pharmacodyn. et de therap. **46:** 192 (Oct. 15) 1933.
18. Phenylaminoethanol Sulfate, J. A. M. A. **91:** 1037 (Oct. 6) 1928.
19. Bertolet, J. A.: Benzyl Methyl Carbinamine Carbonate, M. J. & Rec. **136:** 75 (July 20) 1932.
20. Benzedrine, J. A. M. A. **101:** 1315 (Oct. 21) 1933.
21. Byrne, H. V.: The Use of Benzyl-Methyl-Carbinamine Carbonate in the Treatment of Rhinitis, New England J. Med. **209:** 1048 (Nov. 23) 1933.
22. Wood, E. L.: A New Drug for the Treatment of Eustachian Tube and Middle Ear, Arch. Otolaryng. **21:** 588 (May) 1935.
23. Scarano, J. A.: Rapidity of Shrinkage and Immediate and Secondary Reactions Following Local Applications of Ephedrine and Benzedrine, M. Rec. **140:** 602 (Dec. 5) 1934.
24. Benzedrine Sulfate "Pep Pills," editorial, J. A. M. A. **108:** 1973 (June 5) 1937.
25. Guttmann, Erich, and Sargant, William: Observations on Benzedrine, Brit. M. J. **1:** 1013 (May 15) 1937.
26. The "Confidence Drug," Pharmaceutical J. **138:** 539 (May 22) 1937.
27. Detrick, L. E.; Millikan, Ralph; Modern, F. S., and Thienes, C. H.: On the Pharmacology of Phenylisopropylamine (Benzedrine), J. Pharmacol. & Exper. Therap. **60:** 56 (May) 1937.
28. Pedden, J. R.; Tainter, M. L., and Cameron, W. M.: Comparative Actions of Sympathomimetic Compounds: Bronchodilator Actions in Experimental Bronchial Spasm of Parasympathetic Origin, J. Pharmacol. & Exper. Therap. **55:** 242 (Nov.) 1935.
29. Cameron, W. M., and Tainter, M. L.: Comparative Actions of Sympathomimetic Compounds: Bronchodilator Actions in Bronchial Spasm Induced by Histamine, J. Pharmacol. & Exper. Therap. **57:** 152 (June) 1936.

described by Alles [30] and Alles and Prinzmetal.[31] They referred to their own previous studies (Patek and Thienes [32] and Thienes [33]) and continued the study of the effects of this drug in dogs, cats and rabbits. Their study consisted principally of effects of combinations of benzedrine with other drugs. They believed that benzedrine was proved to be a central nervous system stimulant in anesthetized animals because of the increase in rate and depth of respirations, as well as the struggling and vocalizations observed in their experimental animals. They described a pressor action in all the animals and noted that tachyphylaxis was marked. It was observed that the pressor effect was moderately decreased by cocaine and ergotamine. In low concentrations (10^{-5} or less) benzedrine salts had no effect on excised smooth muscle of rabbits or guinea-pigs and inhibited the intestine of the cat. In high concentrations (10^{-4} or higher) benzedrine caused contraction of all smooth muscle, although a temporary inhibition of cat ileum and duodenum preceded the contraction produced by the benzedrine. This inhibition was prevented by atropine and decreased by nicotine, while the contraction itself was not altered by atropine but was decreased by nicotine. No effect of atropine or nicotine was noted in the responses of rabbit tissues to benzedrine, but the contraction of the guinea-pig intestine was abolished by atropine. Ergotamine abolished epinephrine action on cat duodenum but merely decreased the action of benzedrine. Hydrastinine decreased or abolished the actions of epinephrine and of benzedrine, while yohimbine contracted the intestine but caused negligible alteration of the actions of epinephrine and benzedrine.

Myerson, Loman and Dameshek [34] studied the hematologic properties of benzedrine sulfate and claimed an increase (following the oral administration of therapeutic doses) in red blood cell counts of 1½ to 3 million with doubling, tripling and quadrupling of the leukocyte counts. Recently Simpson [35] has attributed this as with other vasoconstrictors to "the extrusion into the circulation" of these cells "from the storage and hematopoietic centers, including the bone marrow." There was no increase in hemoglobin or immature white cells (except for an occasional increase in neutrophils). Myerson and his associates [34] also studied the basal metabolic rate and found no change following its use. Lagen, Soley and Leake,[36] however, found individual variations which indicate that further study is necessary before it can be said that the drug is without effect on the rate. Peoples and Guttmann [37] did not find any change in the blood sugar levels following the clinical use of this drug. Myerson and his associates [34] also studied the blood sugar levels. They did not encounter change in the size of the pupil or symptomatic change in the gastro-intestinal, respiratory or genito-urinary functions.

Pressor Effects.—Alles [30] found that benzedrine was equal in pressor effect to beta phenylethylamine when injected intravenously in dogs under barbital anesthesia and that it had a much weaker but longer effect than epinephrine. Similar results were obtained with 4 hydroxy- and 3,4 dihydroxy-phenylisopropylamine (4 hydroxy- and 3,4 dihydroxy α-phenyl β-amino propane—see chart) and phenylethylamine. The most prolonged effect and the nearest to epinephrine in initial effect was produced by 3,4 dihydroxy-phenylisopropylamine. The propylamines were found to be much more toxic than the ethylamines but this toxicity was lessened by the introduction of the hydroxy groups to the compounds. Nathanson [38] has experimented with 4 hydroxy phenyl isopropylamine (supplied by the makers of benzedrine) and found it effective in the prevention of cardiac arrest without central nervous stimulation or unpleasant side effects.

Tainter [17] made a very extensive examination of forty-four sympathomimetic amines. He noted that Piness, Miller and Alles [12] and later Alles [30] reported that benzedrine maintained blood pressure at a high level after subcutaneous or oral administration in man and that Hartung and Munch [15] had obtained comparable effects in dogs by injection. Tainter [17] considered the pressor activity of benzedrine high and regular enough to attempt the determination of the possible mechanism. However, he found that he could not employ the usual procedures because the second injection of the drug caused a fall of blood pressure. He avoided this effect by injection of cocaine or ergotamine before administration and then compared responses with those of the controls. He determined that when the epinephrine response was doubled by cocaine the pressor response to this propylamine was abolished and that when the epinephrine response was reversed by ergotamine this compound still gave a good rise of blood pressure.

Many of those who have studied benzedrine clinically have noted its pressor effects. In this connection it is necessary to consider some of the symptomatic and pressor effects of epinephrine. Loman and Myerson [39] noted that epinephrine causes a rise in the intracranial pressure together with a rise of arterial and internal jugular venous pressures and attributed the former to the arterial rise, since there was a vasoconstriction of the cerebral blood vessels. Gibbs, Gibbs and Lennox [40] noted that the cutaneous injection of amounts of epinephrine sufficient to cause a marked rise in blood pressure caused a great increase in cerebral blood flow, this increase undoubtedly being secondary to increase in blood pressure. Minute amounts of epinephrine caused a slight rise in flow without change (or with a fall) in blood pressure suggesting a vasodilator action. Sulman [41] claimed similar pressor and depressor responses in his clinical studies of the inhalation of benzedrine. Anderson and Scott [42] reported both increases and decreases in pulse rate and blood pressure in a series of six cases. Myerson and his associates [43] observed the pressor effects of benzedrine given orally, subcutaneously and intravenously in a special but unusually well controlled series of cases. Most of them were "passive, unemotional cases of dementia praecox who lay perfectly quiet throughout the entire procedure." In eighteen cases from 9 to 50 mg. of the drug was administered subcutaneously and resulted in gradual rises of from 10 to 54 mm. of mercury—reaching a maximum in from eleven to eighty-five minutes and returning to normal in from one and one-half to eight hours. During this period the pulse rate was diminished from 4 to 25 beats per minute in twelve cases, unchanged in four and increased in two. Fourteen patients were then given 40 mg. of benzedrine sulfate by mouth and registered increases of from 8 to 68 mm. of mercury in systolic pressure. The effect was slower than with the subcutaneous administration and the pulse rate was more consistently lowered. The authors administered from 20 to 40 mg. subcutaneously, followed it with from 20 to 30 mg. of acetyl-beta-methyl choline and the effect of the benzedrine was more than counteracted for the period of activity of the choline (from ten to twenty minutes), after which the effects of benzedrine supervened. Further experiments indicated that atropine enhanced the pressor effect of

30. Alles, G. A.: The Comparative Physiological Actions of dl-β-phenylisopropylamines: I. Pressor Effect and Toxicity, J. Pharmacol. & Exper. Therap. **47:** 339 (March) 1933.

31. Alles, G. A., and Prinzmetal Myron: Comparative Physiological Actions of dl-β-phenylisopropylamines; Bronchial Effect, J. Pharmacol. & Exper. Therap. **48:** 161 (June) 1933.

32. Patek, P., and Thienes, C. H.: Smooth Muscle Actions of Epinephrine Substitutes; Primary Phenylalkylamines, Arch. internat. de pharmacodyn. et de thérap. **47:** 241 (March) 1934.

33. Thienes, C. H.: Proc. Soc. Exper. Biol. & Med. **26:** 501, 1929.

34. Myerson, Abraham; Loman, Julius, and Dameshek, William: Physiologic Effects of Benzedrine and Its Relationship to Other Drugs Affecting the Autonomic Nervous System, Am. J. M. Sc. **192:** 560 (Oct.) 1936.

35. Simpson, S. L.: Correspondence, Brit. M. J. **1:** 93 (Jan. 9) 1937.

36. Lagen, J. B.; Soley, Mayo H., and Leake, T. B.: The Effect of Benzedrine on the Basal Metabolic Rate, Proc. Soc. Exper. Biol. & Med. **35:** 276 (Nov.) 1936.

37. Peoples, S. A., and Guttmann, E.: Hypertension Produced with Benzedrine; Its Psychological Accompaniments, Lancet **1:** 1107 (May 16) 1936.

38. Nathanson, M. H.: Action of Para-Hydroxy-Phenyl-Iso-Propyl-amine on Induced Cardiac Standstill, Proc. Soc. Exper. Biol. & Med. **35:** 627 (Jan.) 1937.

39. Loman, Julius, and Myerson, Abraham: Action of Certain Drugs on Cerebrospinal Fluid and on the Internal Jugular Venous and Systemic Arterial Pressures of Man, Arch. Neurol. & Psychiat. **27:** 1126 (May) 1932.

40. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: The Cerebral Blood Flow in Man as Influenced by Adrenalin, Caffeine, Amyl Nitrite and Histamine, Am. Heart J. **10:** 916 (Oct.) 1935.

41. Sulman, L. D.: Certain Conditions in Which Volatile Vasoconstrictor Has Proved of Particular Value—Preliminary Report, M. Times & Long Island M. J. (now called M. Times) **63:** 374 (Dec.) 1935.

42. Anderson, E. W., and Scott, W. C. M.: The Cardiovascular Effects of Benzedrine, Lancet **2:** 1461 (Dec. 19) 1936.

43. Myerson, Abraham; Loman, Julius, and Dameshek, William: Physiologic Effects of Acetyl-Beta-Methyl Choline (Mecholyl) and Its Relationship to Other Drugs Affecting the Autonomic Nervous System, Am. J. M. Sc. **193:** 198 (Feb.) 1937. Footnote 34.

benzedrine and that amytal counteracted the pressor effect when given either before or after the benzedrine. Peoples and Guttmann[37] described increases of systolic pressures lasting from two to four and occasionally to twenty-four hours. This increase was found to be greatest in those with hypotension and there was generally an increase in pulse rate which lasted longer than the blood pressure rise. That clinical results are dependent on this effect is apparently disputed by the finding that pressor effects occurred without results and therapeutic results occurred without pressor effects. However, it has been suggested that there is a definite relationship, although it is not apparent in every case. Guttmann[44] noted that the drug was suitable for experimental alterations of blood pressure because its pressor effect was between that of epinephrine and ephedrine as to the rapidity and intensity of action.

NARCOLEPSY

Uhlrich, Trapp and Vidgoff[45] discussed the use of the drug in narcolepsy and noted the many varied but unproved theories of the etiology of this condition. It is usually considered to be chronic and incurable, but spontaneous recovery without treatment has been reported. Remedies which have been used to relieve the condition include psychotherapy, endocrine medication (thyroid, pituitary) and caffeine.[45] The only remedy which has proved successful to any appreciable degree was ephedrine sulfate, which was first used by Janota.[46]

Uhlrich and his co-workers[45] encountered sleeplessness in a patient given benzedrine inhalations and experimented with it in cases of narcolepsy without success. It was not until Prinzmetal and Bloomberg[47] published their report of its oral use in this condition that they reinstituted their study. Prinzmetal and Bloomberg[47] studied nine cases of narcolepsy, in which complete relief from attacks of sleep and practically complete relief from cataplexy was obtained. They considered it three times as effective as ephedrine in preventing attacks of sleep and noted its efficacy in cases that did not respond at all to ephedrine. A footnote referred to four other successful but less carefully studied cases. The authors did not consider the possible pressor effects of the drug.

Uhlrich and his co-workers[45] used it orally in six cases with consistently good results. They suggested that the difference between the oral and inhalation effects of this drug might be largely a matter of dosage. Peoples and Guttmann[37] confirmed the insomnia-producing effects noted by these workers in treating cases of narcolepsy. (An additional reference to its use in narcolepsy[48] has appeared since the report was formulated.)

MENTAL EFFECTS: MOOD AND FATIGUE

Peoples and Guttmann[37] described the following effects in a group of twenty-five institutionalized patients: "feeling of confidence, elation, and well being . . . happier, brighter, more energetic and free from care and worry." Myerson and Ritvo[49] described "a definite feeling of well being," and later Myerson[50] studied its effect on mood and fatigue in normal and neurotic persons. He described the following results, yet noted that a thorough study of the effects had not been made: Normal nonpsychiatric and non-neurotic persons suffering from fatigue and slight malaise due to insufficient rest received "immediate benefit and relief of a pressor type." He suggested that as an emergency measure the drug was probably of benefit to normal persons. He studied it in certain cases of narcosis associated with depression, fatigue, anhedonia and many stages of psychoses of this type. He stated that the ameliorating effect was neither permanent nor curative, but he noted that it helped to combat morning apathy and depression.

Nathanson[51] noted amelioration of fatigue in 80 per cent of his cases of exhaustion and lessening of migraine in four cases in which this condition was associated with attacks of weakness. He described "a sense of increased energy and capacity for work" in more than half the cases. In addition, "a feeling of exhilaration and sense of well being was a consistent effect" and "patients volunteered that there had been a definite increase in mental activity and efficiency." He also described similar effects of a so-called pick me up nature in fifty-five normal individuals. It must be considered, however, that these results are purely subjective and information received by the Council indicates that this use is ill advised.

Guttmann[44] noted the stimulating and euphorizing effect on normal persons with similar results in depressive patients. He described two groups—one with an initial stage of mild intoxication followed by mild elation similar to that which the second group encountered without the prodromal dizziness or giddiness. This he interpreted to indicate influence on the mood and on the psychomotor retardation. These effects could not be entirely correlated with the pressor effect, since they occurred even when a depressor effect ensued, but he believed there was a close relationship. Guttmann[44] also suggests a possible interrelationship between the effect on mood and the effect on sleep.

GASTRO-INTESTINAL EFFECTS

Myerson and Ritvo[49] described the effect of this drug on spasm of the gastro-intestinal tract. They found that it was of value in diminishing or abolishing the spasm when due to whatever cause, such as unpleasant emotion, organic disease of the gastro-intestinal tract and reflex spasm (spastic colitis and pylorospasm) due to disease elsewhere in the body. It was found that the drug facilitated x-ray study of the gastro-intestinal tract and was useful in differentiating functional and organic spasm. Later Ritvo[52] noted that, when given orally or by injection, the drug is sympathomimetic in character and that results of its use include relaxation of the spasm of stomach, pylorus and intestine. This permits better roentgenographic study of the stomach and duodenum. The tonus of the stomach is lessened, but peristalsis is diminished only slightly. The colon becomes widened, the haustrations diminish in number and depth, and spastic deformities of the bowel disappear. The patient is able to retain the opaque enema with less discomfort.

OTHER CLINICAL USES

A preliminary report of the use of benzedrine in the control of blood pressure during spinal anesthesia has been issued by the Mayo Clinic.[53] In a series of twenty-six cases involving operation on the urinary tract, benzedrine was given by inhalation. There was a resultant mild pressor action in twenty-three cases. It was necessary to give the drug before the decrease in blood pressure became alarming because of the lag between administration and pressor effect.

Its effect on intelligence scores (Cattell test) in certain institutionalized patients has been studied by Sargant and Blackburn.[54] The results show some increase in score. The authors felt that the drug had more effect on those suffering from pure emotional upsets than on the schizophrenic.

DOSAGE

The dosages used in the experimental and the early clinical work were as follows:

Prinzmetal and Bloomberg[47] used from 10 to 40 mg., Uhlrich and his co-workers[45] from 20 to 50, Peoples and Guttmann[37] from 10 to 80, Myerson and Ritvo[49] from 10 to 40, Myerson[50] from 5 to 20 and Piness, Miller and Alles[12] 50 mg. Nathanson[51] used from 10 to 20 mg. in the morning in

44. Guttmann, E.: Effect of Benzedrine on Depressive States, J. Ment. Sc. **82**: 618 (Sept.) 1936.
45. Uhlrich, Helmuth; Trapp, C. E., and Vidgoff, Ben: The Treatment of Narcolepsy with Benzedrine Sulfate, Ann. Int. Med. **9**: 1213 (March) 1936.
46. Janota, O.: Symptomatische Behandlung der pathologischen Schlafsucht, besonders der Narkolepsie, Med. Klin. **27**: 278 (Feb. 20) 1931.
47. Prinzmetal, Myron, and Bloomberg, Wilfred: The Use of Benzedrine for the Treatment of Narcolepsy, J. A. M. A. **105**: 2051 (Dec. 21) 1935.
48. Shapiro, M. J.: Benzedrine in the Treatment of Narcolepsy, Minnesota Med. **20**: 28 (Jan.) 1937.
49. Myerson, Abraham, and Ritvo, Max: Benzedrine Sulfate and Its Value in Spasm of the Gastro-Intestinal Tract, J. A. M. A. **107**: 24 (July 4) 1936.
50. Myerson, Abraham: Effect of Benzedrine Sulfate on Mood and Fatigue in Normal and in Neurotic Persons, Arch. Neurol. & Psychiat. **36**: 816 (Oct.) 1936.
51. Nathanson, M. H.: The Central Action of Beta-Aminopropylbenzene (Benzedrine) Sulfate, J. A. M. A. **108**: 528 (Feb. 13) 1937.
52. Ritvo, Max: Drugs as an Aid in Roentgen Examination of the Gastro-Intestinal Tract, Am. J. Roentgenol. **36**: 868 (Dec.) 1936.
53. Control of Blood Pressure During Spinal Anesthesia—A Preliminary Report on the Use of Benzedrine, Proc. Staff Meet., Mayo Clin. **37**: 585 (Sept. 9) 1936.
54. Sargant, W., and Blackburn, J. M.: The Effect of Benzedrine on Intelligence Scores, Lancet **2**: 1385 (Dec. 12) 1936.

the treatment of exhaustion. Subsequent evidence indicates that there is considerable variability in the response of individual patients. It is advisable, therefore, to institute treatment with from 2.5 mg. to 10 mg. and increase this dosage up to not more than 20 mg. three times a day, depending on the necessity of increasing the dosage to obtain a therapeutic response.

REACTIONS AND CONTRAINDICATIONS

Doses which caused reactions were usually those which were greater than the amount necessary to produce therapeutic effects.

A correspondence item in THE JOURNAL [55] suggested that continued administration may result in a pressor effect. Sleeplessness has been encountered with the overdosage with the inhaler and the solution.

Overdosage and sometimes therapeutically effective doses of benzedrine sulfate have resulted in many reactions. Prinzmetal and Bloomberg [47] encountered insomnia, hyperexcitability (overstimulation of the central nervous system with dilated pupils and inability to relax). Uhlrich and his co-workers [45] encountered nausea, anorexia and in one case an extramenstrual period. Myerson and Ritvo [49] encountered unpleasant effects in 2 per cent of their 200 patients, including chills, nausea, restlessness and diarrhea, all within several hours after administration. Myerson [50] noted the restlessness and sleeplessness resulting from the administration of the drug orally in the afternoon.

Nathanson [51] described a tendency to loquaciousness. Ten patients noted a marked loss of appetite and definite reduction in weight. Occasionally secondary depression followed initial stimulation. Dryness of the mouth, disturbed sleep, transitory tremor of the hands, sweating and palpitation—usually of short duration—were noted. The drug was discontinued in three cases because of sleeplessness (in two) and severe palpitation (one). He did not encounter a rise in arterial pressure; he found no extrasystoles except in one case; four patients having extrasystoles showed no additional cardiac effect from the drug. He goes so far as to point out that the use of the drug may lead to harmful results in that patients may overdo without receiving the warning of fatigue. He also recommends administration under the physician's prescription only. He notes that complete indications and contraindications are not yet available.

Apparently there is no tolerance, as response has been found to be the same after fourteen months' use in one case and after shorter periods in other cases. Wilbur, MacLean and Allen [56] noted that in their opinion the drug should not be used continuously unless the patient is less than 60 years of age, has no evidence of cardiovascular disease, and can be closely watched. Others have suggested that cumulative effects may be deleterious. Anderson and Scott,[42] noting no record of severe cardiovascular effects produced by benzedrine, reported an unusual case in which the patient went into collapse after 30 mg. of benzedrine. They recommended that, until more precise knowledge of the cardiologic effects of benzedrine is obtained, caution should be exercised in the administration of doses of from 10 to 20 mg. or more, particularly in elderly subjects.

SUMMARY

After consideration of the available evidence, the Council declared that the permissible claims for the usefulness of Benzedrine Sulfate should not exceed the following stipulations:

Narcolepsy.—Benzedrine Sulfate is useful for the treatment of narcolepsy and for controlling symptoms similar to those of narcolepsy in the treatment of postencephalitic parkinsonism. Its use is not recommended in the treatment of sleepiness and fatigue in normal individuals because of the possible danger of pressor effects from continued use, the dangers of eliminating the warning signal of sleepiness in individuals who are overdoing, because of the possibility of habit formation or addiction from such use and because cases of collapse have ensued when the drug has been used for this purpose.

Mental Effects: Mood and Fatigue.—Benzedrine Sulfate is useful in the treatment of certain depressive psychopathic conditions. Its use is not recommended for developing a sense of increased energy or capacity for work, or a feeling of exhilaration or as a "pick-me-up" in individuals other than those under the strict supervision of the physician. The Council believes that its use for these purposes should be confined to institutions, since the dangers involved in the use of the drug for this purpose in those going about their daily tasks are similar to the dangers mentioned in connection with fighting off sleep.

Gastro-Intestinal Effects.—Benzedrine Sulfate is useful in facilitating roentgenographic study of the gastro-intestinal tract, but it is not recommended at present for use in the treatment of spastic colitis and pylorus spasm.

Other Clinical Uses.—Further evidence is necessary before serious consideration can be given to these various other applications of this agent to therapeutics.

Reactions and Contraindications.—The very nature of the therapeutic effects as well as side actions of this drug requires that its use be promoted with proper cautionary statements as to pressor effect, hyperexcitability, gastro-intestinal disturbance, restlessness and sleeplessness and in overdosage, chills, collapse and syncope. It should also be carefully noted that the drug is contraindicated in those having cardiovascular disease, especially when hypertension is a sequence of that disease.

Dosage.—The use of the drug should be instituted with a dose of 2.5 mg. to 10 mg., and it is recommended that no single dose exceed 20 mg. In certain conditions it may be necessary to repeat the use of the drug two or three times daily. It is preferable, if possible, to administer the effective quantity during the morning.

CONCLUSION

The Council declared that Benzedrine Sulfate (Smith, Kline & French) and the submitted dosage form would be accepted for inclusion in N. N. R. provided the firm agrees to limit the claims for the usefulness of the drug to the treatment of narcolepsy and postencephalitic parkinsonism; to limit the claims for its usefulness in depressive mental states to the stipulations of this report; and, further, provided there are no other conflicts with the rules.

55. Morse, Withrow: Effects of Benzedrine on Blood Pressure, Correspondence, J. A. M. A. **107**: 1582 (Nov. 7) 1936.

56. Wilbur, D. L.; MacLean, A. R., and Allen, E. V.: Clinical Observations on the Effect of Benzedrine Sulfate, Proc. Staff Meet., Mayo Clin. **12**: 97 (Sept. 17) 1937.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

CALCIUM GLUCONATE (See New and Nonofficial Remedies, 1937, p. 150).

Calcium Gluconate Effervescent-Flint: Each gram contains calcium gluconate-U. S. P. 0.5 Gm., citric acid 0.25 Gm., and sodium bicarbonate 0.25 Gm.

Dosage:—Orally, for adults, 10 Gm. (150 grains) three times a day; for children, 4 Gm. (60 grains) three times a day.

Manufactured by Flint, Eaton & Co., Decatur, Ill. U. S. patent 1,983,954. No U. S. trademark.

Calcium gluconate effervescent occurs as a white, coarsely granular, odorless material, with a biting acid taste. Its solubility in water is not less than 28 Gm. per hundred cubic centimeters at 25 C.; the resulting solution is acid to litmus. The loss in weight over sulfuric acid is not greater than 0.5 per cent. The product conforms to tests for purity of calcium gluconate-U. S. P.; the calcium oxide content is not less than 6.0 per cent nor more than 6.4 per cent.

Dissolve approximately 5 Gm. of calcium gluconate effervescent, accurately weighed, in water to make 100 cc. of solution; transfer a 25 cc. portion to a 250 cc. beaker, boil for two minutes and, while boiling, add 25 cc. of a hot saturated solution of calcium hydroxide and continue boiling for five minutes; digest on the steam bath for two hours and filter while hot through a hot Gooch crucible, wash the residue with boiling water and dry to constant weight at 100 C.: the citric acid content is not less than 24.5 per cent nor more than 25.8 per cent. Dissolve approximately 10 Gm. of calcium gluconate, effervescent, accurately weighed, in water to make 100 cc. of solution; transfer a 25 cc. portion to a suitable Erlenmeyer flask, boil for two minutes, cool, and titrate with tenth-normal sodium hydroxide using phenolphthalein as an indicator: a 1 Gm. sample requires not less than 7 cc., nor more than 7.6 cc. of tenth-normal sodium hydroxide. Transfer about 0.1 Gm. of calcium gluconate effervescent, accurately weighed, to a 150 cc. beaker and dissolve in 5 cc. of distilled water; cool the beaker and contents in ice water and add 25 cc. of a 15 per cent magnesium uranyl acetate solution; place the mixture in an ice bath at 20 C. and allow to stand for twenty-four hours; filter with suction and wash with 95 per cent alcohol saturated with sodium magnesium uranyl acetate; dry the precipitate at 110 C. for thirty minutes, cool and weigh: one Gm. of sodium magnesium uranyl acetate being equivalent to 0.0153 Gm. of sodium, the sodium content is not less than 6.4 per cent nor more than 7.0 per cent.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, DECEMBER 18, 1937

ESSENTIAL AMINO ACIDS IN NUTRITION

Of the twenty-two amino acids commonly obtained by the hydrolysis of proteins, ten are now known to be essential for growth and twelve are considered nonessential. Such is the brief announcement [1] that provides the concluding chapter to a series of brilliant researches conducted at the University of Illinois for more than the last decade but having their origin earlier in the contributions of Osborne and Mendel. The latter workers showed more than twenty years ago that proteins differed in their nutritional value. Animals could not grow when restricted to a diet in which the sole source of protein was zein or gliadin, the alcohol soluble proteins of corn and wheat respectively. Zein is a peculiar protein in that it contains neither tryptophan nor lysine, and gliadin contains only small amounts of lysine. The addition of the amino acids in which each of these proteins is deficient promoted normal growth, and it was concluded that tryptophan and lysine must be furnished by the diet in order that growth might occur. Evidence was also obtained to show that aminoacetic acid, if needed by the body for growth, can be formed from other sources and therefore need not be included in the diet. Proteins accordingly could be divided into complete and incomplete proteins, depending on whether they provided all the indispensable amino acids or were deficient in one or more of these. This method of study was hampered by the relatively few proteins that had been isolated in pure form and were adaptable for feeding experiments.

The next advance in the study of the nutritive value of the individual amino acids came as a result of the substitution of protein hydrolysates for the protein in the diet. Proteins such as casein could be treated with acids and thus converted to their component amino acids. It was necessary, of course, to remove the mineral acid usually employed to effect the hydrolysis and to add some substances, such as tryptophan, which are destroyed during the treatment. From the mixture of amino acids that comprise a hydrolyzed protein, groups of amino acids would be removed and others added. By this technic it was found that histidine is another amino acid which is essential for growth. The limitation to this method of procedure was the difficulty of chemically separating the amino acids.

The obvious possibility of feeding mixtures of pure amino acids remained an unattainable goal until Rose and his collaborators at the University of Illinois began an extensive program of preparing and accumulating all the known amino acids in quantities sufficient to permit feeding mixtures of them to rats. Numerous difficulties were encountered along the way, but one by one they were successfully overcome. Then it was learned that the feeding of all the known amino acids, including methionine, which had been discovered by Mueller in 1922, failed to promote growth. The addition to the diet of a small amount of protein, insufficient in itself to promote growth, gave good results. The bold prediction was made that in proteins there must be some amino acid which at that time had not been discovered, that this unknown amino acid was indispensable for growth and that it was present in some proteins in higher concentration than in others. An intensive study was begun at once to learn the nature of the hypothetical amino acid which had eluded the attention of all other investigators in the field of protein chemistry. Various proteins were hydrolyzed and fractionated by different chemical means, and the fractions tested for their growth promoting properties when added to mixtures of amino acids; eventually, from a potent fraction, the amino acid itself was isolated. Further work led to its identification as one of the four possible alpha-amino-betahydroxybutyric acids. To the naturally occurring form of this indispensable amino acid its discoverers have given the name threonine.

Having thus obtained a knowledge of all the amino acids in ordinary proteins, Rose and his collaborators were able to continue their experiments with the hope of attaining a successful solution to the problem of the nutritional importance of each amino acid. When all the amino acids were fed, including threonine, good growth was obtained. Individual amino acids were omitted from this mixture and the effect on the growth of the animals was observed. The dénouement of the story thus developed rapidly. The twenty-two common amino acids now can be classified precisely according to their growth effects. Among the essential amino acids are lysine, tryptophan, histidine, phenylalanine, leucine, isoleucine, threonine, methionine and valine. Arginine, which at one time was thought to be nonessential, should also be classified as an essential amino acid because the animal body cannot synthesize this substance at a rate fast enough to permit normal growth. The nonessential amino acids are aminoacetic acid, alanine, serine, norleucine, aspartic acid,

1. Rose, W. C.: The Nutritive Significance of the Amino Acids and Certain Related Compounds, Science **86**: 298 (Oct. 1) 1937.

glutamic acid, hydroxyglutamic acid, proline, hydroxyproline, citrulline, tyrosine and cystine. For many years cystine was thought to be an essential amino acid. Later work has made clear that the other sulfur containing amino acid of proteins, methionine, is essential for growth but that cystine is not. However, if the amount of methionine in the diet was not sufficient to permit normal growth, it was observed that the addition of small amounts of cystine would accelerate growth. It has been suggested that methionine forms some substance which also can be formed from cystine and that this derivative is necessary in order that growth can occur. To a limited extent, therefore, cystine can replace a portion of the methionine in the diet.

This work on the nutritional significance of the amino acids has come to fruition so rapidly that it is difficult to grasp all the possibilities that the future portends. It has been suggested that a method might be developed for the study of the origin of each of the dispensable amino acids and of the chemical conversions involved in their formation. The amino acids obtained from foods are utilized by the body for the formation of the proteins of the blood and tissues and for the production of some of the hormones and other substances that contain nitrogen. The chemical changes that take place in the body are exceedingly important in health and in disease, and work of the kind reported by the Illinois investigators will lead eventually to a firmer understanding of some of the numerous transformations undergone by the important nitrogenous components of the body.

GRADUATE INSTRUCTION IN SYPHILIS CONTROL WORK

The Advisory Committee to the U. S. Public Health Service which outlined a venereal disease control program for state and local health departments [1] agreed on the importance of the postgraduate instruction of practicing physicians in the clinical management and public health control of syphilis and gonorrhea. Two types of training are to be fostered, the short review course in current diagnostic and therapeutic practice and prolonged intensive training in venereology for the specialist.

Because of the need for the assistance and cooperation of the physician in private practice with the health department, the U. S. Public Health Service has made a special attempt to provide postgraduate training for physicians in the fundamentals of the clinical management and public health control of syphilis, gonorrhea and the other venereal diseases. Special allotments of funds, appropriated under the provisions of the Social Security Act, have been made to a number of states.

Special allotments have been made to the state health officers of California, Massachusetts, New York, Ohio and Tennessee for the development of a special postgraduate course in venereal disease control work. Under this plan the course of postgraduate training is organized by the state health officer and the authorities in the medical school that is selected. The training is intended primarily for health officers and for private physicians who cooperate with state and local departments of health. Applicants to be eligible for training must be nominated by the state health officer of the state from which they come. Except for nominal registration fees in one or two medical schools, the training is provided without charge. It is hoped that the medical schools which have been selected will serve health officers and physicians from all the states which are conveniently located in that part of the country.

More than a year ago a special course of training in syphilis control work was developed in the Johns Hopkins University School of Medicine with funds allotted by the Public Health Service to the Maryland State Department of Health. Shortly thereafter a course of training was developed through the utilization of Social Security funds by the Pennsylvania State Department of Health in cooperation with the University of Pennsylvania. The latter course is for the purpose of training physicians, public health nurses and medical social workers in case finding and case holding methods as they pertain to the control of the venereal diseases.

For the Negro physician a special allotment has been made to the District of Columbia Health Department and a course has been developed at Howard University. Negro physicians nominated by state health officers are eligible for this postgraduate training at very small cost.

The magnitude of the venereal disease problem in this country is such as to require the full cooperation of the medical profession if success is to be attained. The short review courses recently organized, in which the modern clinical management of the venereal diseases is taught, will not qualify the physician in general practice as a finished specialist. Present facilities for the training of specialists are not available to provide entirely for the care of the large number of patients infected with syphilis and gonorrhea who now require medical attention. However, there is no reason why the physician in general practice should not treat the average patient with early and latent syphilis unless special complications develop, which indicate the need for consultation with an expert. To be able to take on this new duty, however, it is essential that the general practitioner know the fundamentals of the management of syphilis and be aided by his health department. Every health officer and every physician interested in the control of syphilis and gonorrhea should see that those who diagnose and treat these diseases know the basic principles. The postgraduate courses of training that have been developed should be utilized to their fullest extent.

1. Recommendations for a Venereal Disease Control Program in State and Local Health Departments, Report of an Advisory Committee to the United States Public Health Service, Ven. Dis. Inform. **17**: 1 (Jan.) 1936.

THE CHANGE OF PROTEIN TO CARBOHYDRATE

Claude Bernard's discovery in 1848 of glycogen in the liver had far reaching significance. Not only had he demonstrated a "nouvelle fonction du foie" but through the experimental approach employed he opened a question of fundamental significance in intermediary metabolism; he offered convincing evidence of the transformation of protein to carbohydrate in the animal organism. Soon after the announcement of this new function of the liver, somewhat similar cogent evidence of the change of carbohydrate to fat was developed by Lawes and Gilbert. The fundamental nature of protein metabolism compelled investigators in this field to consider seriously the extent of the metabolic transformation of protein to sugar. Aminoacetic acid was shown to increase the hepatic glycogen in fasting rabbits. Studies on diabetic patients showed that some two thirds of the meat and gelatin fed appeared as urinary sugar. Later it was demonstrated that aminoacetic acid, alanine and asparagin were changed to sugar in the depancreatized dog. The subject was greatly extended by Graham Lusk, who used phlorhizinized dogs as experimental subjects. Largely on the basis of his studies the then known amino acids were divided into the glycogenic and nonglycogenic amino acids. From the foregoing investigations as well as others employing as criteria the change in respiratory quotient and the antagonism to insulin hypoglycemia, the current view accepts aminoacetic acid, alanine, serine, aspartic acid, glutamic acid, cystine, methionine, proline and arginine as glycogenic amino acids.

Recently a renewal of interest in this question has emphasized the importance of details of chemical structure of the amino acids, a factor not heretofore appreciated. Criticizing the use of phlorhizin as unphysiologic, Butts and his co-workers[1] have employed the effect on artificial ketosis induced in experimental animals by oral administration of sodium acetoacetate as well as the change in amount of liver glycogen brought about by optically active forms of the amino acids. It was found that aminoacetic acid, early recognized as an important glycogenic amino acid, is inferior in this respect as well as in ketolysis to both *dl*-alanine and *d*-alanine. The latter compound, the naturally occurring form of alanine, is superior to the others. As ketolytic substances *l*-aspartic acid, *d*-glutamic acid and *dl*-aspartic acid are all inferior to *dl*-alanine, whereas *l*-aspartic acid, *dl*-aspartic acid, *d*-glutamic acid and *dl*-glutamic acid are glycogenic in the order named.

Of considerable interest are the observations on the various leucines. Leucine has persistently given negative results in experiments on glycogenesis; in these more quantitative studies it again failed to yield carbohydrate and was converted to acetone bodies. Glycogen was formed by *dl*-isoleucine and by *dl*-norleucine and the latter was also ketolytic. These observations are interesting in the light of the recent demonstration of the essential nature of leucine and isoleucine; it would appear that their indispensability does not rest primarily on the metabolism of the non-nitrogenous portion of the molecule. These newer observations on the correlation between the finer details of the structure of amino acids and their metabolic change to carbohydrate emphasize again the extraordinary specificity of biologic processes. In time they may exert unsuspected influence on the conceptions and treatment in the field of internal medicine.

1. Butts, J. S.; Dunn, M. S., and Hallman, Lois F.: J. Biol. Chem. **112**: 263 (Dec.) 1935. Butts, J. S.; Blunden, Harry, and Dunn, M. S., ibid. **119**: 247 (June) **120**: 289 (Aug.) 1937.

Current Comment

CANADIAN EXPERIENCE WITH ZINC SULFATE SPRAYS FOR PREVENTION OF POLIOMYELITIS

The serious outbreak of poliomyelitis in and around Toronto this year afforded an exceptional opportunity for the study of the prophylactic value of zinc sulfate sprays. The report by Tisdall and his co-workers[1] on this subject deserves careful study. A trial of nasal spraying was approved by the Department of Health of Ontario on August 29. It was agreed that each child should be sprayed on two occasions, ten or twelve days apart, and that from 0.5 to 1 cc. of the solution should be placed in each naris in each spraying. The solution contained 1 per cent zinc sulfate, 1 per cent pontocaine and 0.5 per cent sodium chloride. The spraying was done according to the technic of Peet, Echols and Richter but differed from their recommended procedure in that it was not administered on three successive days, since this method was considered impracticable. The peak of the epidemic occurred during the week ended September 4. The first spraying, begun on August 31 and completed by September 5, was performed by forty-four attending otolaryngologists of eight hospitals in the city. In the period of one week from the authorization of the study, 5,233 children had received the first spraying. The second spraying extended from the 13th to the 16th of September. No serious complications occurred. Nine hundred and nine tests, representing 740 children, were made to determine the number who had lost their sense of smell. From these observations it would appear that some 25 per cent had anosmia. A representative control group of 6,300 children was obtained in the city proper. Among the 4,713 children who were sprayed twice, eleven cases of poliomyelitis occurred up to October 12, thirty days from the second spraying. One of these occurred six days after the first spraying and was not included in the analysis. In the control group of 6,300 children, eighteen cases occurred. The attack rate in the period from seven days after the

1. Tisdall, F. F.; Brown, Alan; Defries, R. D.; Ross, M. A., and Sellers, A. H.: Zinc Sulfate Nasal Spray in the Prophylaxis of Poliomyelitis, Canad. Pub. Health J. **28**: 523 (Nov.) 1937.

first spraying to thirty days after the second spraying was 2.1 in the sprayed group and 2.9 in the control group. The difference is not statistically significant. In the total of the city and suburban groups, the attack rates were 2.9 in the control group and 1.8 in the sprayed group, which also was found not to be statistically significant. The report concludes that since the spraying method employed in this study must be conducted by otolaryngologists or other physicians especially trained in intranasal treatment, requires special facilities and cannot be done quickly enough to meet the emergency of an outbreak, it cannot be considered a practical public health procedure.

HEPATIC FUNCTION AND VITAMIN D

In 1933 Gerstenberger[1] concluded from clinical evidence that the action of antirachitic vitamin D is in some unknown way mediated through the liver. Walter Heymann[2] of the Babies and Children's Hospital, Cleveland, has recently attempted to confirm this conclusion by a study of the effect of experimental hepatic insufficiency on vitamin D therapy in rachitic animals. Rickets was caused and maintained in rats by means of the Steenbock rachitogenic diet. Experimental biliary cirrhosis was produced in one group of rachitic rats by double ligation and transection of the common bile duct. Severe hepatic injury was produced in other groups by intramuscular injections of carbon tetrachloride. Heymann found that from ten to twelve times the routine therapeutic dose of vitamin D was necessary to cure rickets in his biliary cirrhotic group and from two to three times the normal therapeutic dose in the carbon tetrachloride group. In further support of the Gerstenberger theory, Heymann showed that the jaundice associated with experimental hepatic cirrhosis does not impair the calcifying function of the bone. While Heymann's experimental data are susceptible of several interpretations, they do seem to show that normal liver function has an adjuvant part in vitamin D therapy.

Association News

RADIO BROADCASTS

The American Medical Association and the National Broadcasting Company present the fifth series of network health programs, beginning Oct. 13, 1937, and running weekly through June 15, 1938. The programs will be presented over the Red network each Wednesday at 2 p. m. eastern standard time, 1 p. m. central standard time, 12 o'clock noon mountain standard time and 11 a. m. Pacific standard time.

The dates and topics of the broadcasts for the coming month are as follows:

Diet

December 22—Milk from Farm to Table: the production, transportation, pasteurization and home care of milk; its place in the diet; processed milks.

December 29—Dietary Fads: facts vs. fallacies in relation to prevalent false notions on diet.

Contagious Diseases

January 5—Sneezes and Sniffles: cause, spread, prevention of colds, pneumonia and influenza; importance of early medical care.

January 12—Scarlet Fever, Measles and Whooping Cough: modern attitudes toward these diseases; their prevention by community cooperation.

The stations on the Red network are privileged to broadcast the program but, since it is a noncommercial program, they are not obliged to do so. Interest on the part of medical societies, woman's auxiliaries and others may have weight with program directors of local stations. A personal visit to the program director might be advisable if the program is not being taken by a local station. This is an opportunity for the appropriate committees of county medical societies to indicate their interest in having this program broadcast in their community and to enlist the interest of other groups.

1. Gerstenberger, H. J.: Monatschr. f. Kinderh. **56**: 217, 1933.
2. Heymann, Walter: Proc. Soc. Exper. Biol. & Med. **36**: 812 (June) 1937.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

Annual Reregistration Due January 1.—Every licentiate of the Arkansas Eclectic Medical Examining Board must register annually with the secretary of the board between January 1 and the last day in February and pay a fee, if a resident of Arkansas, of $2 and, if a nonresident, of $4. The failure of a licentiate to pay the required fee by March 1 automatically suspends his right to practice while delinquent. If he fails for three successive years to pay the required fee, his license is to be canceled, and thereafter he will be reinstated only on such a showing to the board of moral character and professional qualifications as would entitle the applicant to the issuance of an original license and the payment of the same fee as is required for the issuance of an original license.

CALIFORNIA

Plague Infection in Squirrels in Fresno County.—Under date of November 5, Dr. Walter M. Dickie, director of the state department of health, reported that plague infection had been proved by animal inoculation in fleas from forty-six golden mantled squirrels collected September 30 in the Cedar Crest area, two miles west of Lake Shore, Huntington Lake, Fresno County, according to *Public Health Reports*.

Society News.—Dr. Morris Fishbein, editor of THE JOURNAL, Chicago, addressed the Los Angeles County Medical Association December 2 on "Medicine and the National Policy." A dinner in his honor preceded the meeting.——A symposium on the treatment of dementia praecox was presented before the Society of Neurology and Psychiatry of Los Angeles, December 15, by Drs. Eugene Ziskind, Los Angeles; David W. Lester, Compton; Cullen Ward Irish, Los Angeles; Douglas R. Dodge, Pasadena; John B. Doyle and Samuel D. Ingham, Los Angeles.

CONNECTICUT

Annual Registration Due During January.—Every practitioner of medicine and surgery holding a license to practice in Connecticut is required by law to register during January, with the state department of health, and at that time to pay a fee of $2. Licentiates who have retired from active practice or who live out of the state must register annually but need not pay a fee. A practitioner failing to register is liable to a fine of not more than $5.

Society News.—Dr. Samuel H. Epstein, Boston, addressed the New London County Medical Association October 7 at Norwich on "Treatment of Neurosyphilis."——The Middlesex County Medical Association was addressed in Middletown October 12 by Dr. Richard H. Overholt, Boston, on "Surgical Diseases of the Chest."——At a meeting of the Tolland County Medical Association in Somers, October 19, Dr. C. Charles Burlingame, Hartford, discussed psychiatric problems.

Aid for Crippled Children.—Under the social security act, Connecticut will receive $60,000 from the federal government to be added to a similar amount appropriated by the last session of the general assembly for the state's crippled children program, according to the *New England Journal of Medicine*. The program will include the establishment of five permanent diagnostic clinics throughout the state so that they may be accessible to districts where their services are most needed.

GEORGIA

Personal.—Dr. Isham W. Irvin, Albany, received a silver service from the Dawson Kiwanis Club as a token of appreciation for his work in behalf of unfortunate children in Dawson and Terrell County, according to the state medical journal.

Resolution About Anesthesia.—A resolution was adopted by the Fulton County Medical Society November 18 asking that the Medical Association of Georgia, Georgia Hospital Association, University of Georgia School of Medicine and Emory University be petitioned to take action to improve the science of anesthesia. The society disapproved the sale to the public of the services of salaried, nonprofessional anesthetists.

Society News.—Dr. Evert A. Bancker Jr. discussed "The Electrocardiogram and Its More Common Abnormalities in Man" before the Fulton County Medical Society, Atlanta, November 18. Dr. Martin T. Meyers presented a paper before the society, November 4, entitled "Air Injection in Joint Diagnosis."——Dr. Lewis H. Oden Jr., Blackshear, discussed "The Raw Apple Diet in Infantile Diarrhea" before the Ware County Medical Society in Waycross, October 6.——Papers were presented before the Georgia Medical Society in Savannah, October 26, by Drs. Claude M. Burpee, Augusta, and Walter E. Brown, Savannah, entitled "The Treatment of Gonococcus Infections of the Genital Tract in Girls" and "Unusual Tumor of the Ovaries, Bilateral."——The state board of health opened branch laboratories at Albany and Waycross recently.

ILLINOIS

New County Sanatorium.—Dr. Charles K. Petter of the staff of the Glen Lake Sanatorium, Oak Terrace, Minn., has been appointed director and supervisor of the Lake County Tuberculosis Sanatorium shortly to be erected. He will take office about January 1. The voters of the county approved at the November 1936 election a proposition to build a tuberculosis sanatorium with tax revenue to be collected over a period of ten years starting next summer, newspapers report.

Chicago

Outbreak of Smallpox.—Six cases of smallpox were discovered in the Roseland district, December 11, according to the Chicago *Tribune*. Four of the patients were members of one family and the other two were neighbors. None of the patients have been vaccinated successfully, it was stated. These are the first cases of smallpox reported in the city since April.

Mobile X-Ray Unit.—The Chicago Tuberculosis Institute and the Municipal Tuberculosis Sanitarium are sponsoring a traveling x-ray unit to combat tuberculosis among school children in Chicago. The unit was put into service at the Spalding School for Crippled Children recently. It contains dressing rooms and equipment for taking 400 x-ray plates a day and will be moved from school to school, newspapers reported.

KANSAS

Personal.—Drs. Willard W. Nye, Ebberly J. Leigh, George C. McKnight, all of Hiawatha, and Henry J. Deaver, Sabetha, were guests of honor at a dinner given by the Brown County Medical Society in Hiawatha, November 5. They are all honorary members of the society.——Dr. Charles M. Starr, Larned, has been appointed health officer of Pawnee County.

Society News.—The Golden Belt Medical Society was addressed October 14 in Salina by Drs. James A. Simpson, Salina, on "Podalic Version"; Harry R. Wahl, dean and professor of pathology, University of Kansas School of Medicine, "Multiple Tumors of the Sympathetic Nervous System"; Ralph H. Major, Kansas City, Mo., "Nephritis and Nephrosis," and Frank R. Teachenor, Kansas City, Mo., "Traumatic Injuries of the Head." Dr. Major spoke at the dinner on "Hippocrates and the Isle of Cos."——At a meeting of the Pratt County Medical Society in Pratt, October 22, Dr. Newman C. Nash, Wichita, discussed the treatment of infections with x-rays, and Dr. Albert R. Hatcher, Wellington, anemia due to malignancy in the small intestine.——Dr. Howard E. Snyder, Winfield, addressed the Cowley County Medical Society in Arkansas City, October 21, on "Treatment of Fractures of the Lower Extremities."——At a meeting of the Anderson County Medical Society in Garnett October 20 Drs. Ralph E. White and Ray D. Fraker, both of Garnett, discussed injection treatment of hernia and the use and danger of sulfanilamide, respectively.

LOUISIANA

The Stanford E. Chaillé Memorial Oration.—Dr. Walter Timme, professor of clinical neurology, Columbia University College of Physicians and Surgeons, New York, delivered the twelfth annual Stanford E. Chaillé Memorial Oration before the Orleans Parish Medical Society, New Orleans, December 6. Dr. Timme discussed "Status Hypoplasticus: Its Bearing on All Fields of Medicine and the Automatic Compensatory Mechanisms Involved."

The Rudolph Matas Medical Library.—The library of Tulane University of Louisiana School of Medicine, New Orleans, was named in honor of Dr. Rudolph Matas, emeritus professor of surgery at the university, November 29. The special ceremonies paid tribute to Dr. Matas's years of service to the university and to his constant interest in the development of the library. It also marked his seventy-seventh birthday, which occurred September 12. The medical library is in the Hutchinson Memorial Building and numbers in its collection about 30,168 bound volumes, 2,500 original pamphlets, 1,500 mounted portraits, 60,000 reprints, 250 medical bookplates, and an extensive collection illustrating medicine in art. The library receives currently more than 350 medical periodicals, many of them through the Maurice Stern Fund. Three special collections are the Feingold Library of Ophthalmology, the Kells Library of Dentistry and the recently established Isaac Ivan Lemann Collection on Diabetes. Two small rooms were used for a library and reading room as far back as 1843, when the university was the University of Louisiana. In 1893 the Richardson Memorial Building provided space for the library and in 1896 Dean Stanford E. Chaillé, with two assistants, began the first definite organization of a medical library. The library of the Orleans Parish Medical Society is administered with the Rudolph Matas Medical Library. At the recent dedication Rufus Carrollton Harris, president of the university, presided, and Dr. Charles C. Bass, dean of the medical school, gave the principal address. Dr. Matas graduated at Tulane in 1880 and was associated with it from 1895 to 1927.

MICHIGAN

Changes in Health Officers.—Dr. Thomas E. Gibson, Flint, recently resigned as health officer of Genesee County to accept a similar position in Eaton County to succeed Dr. Joseph W. Davis, formerly of Charlotte, resigned. Dr. Leslie V. Burkett, Midland, formerly health officer of Midland County, has been appointed in Genesee County. Dr. Hugh B. Robins, Marshall, associate director of the Calhoun County Health Department, has been placed in charge of the department, succeeding Dr. Matthew R. Kinde, who is now at the W. K. Kellogg Foundation, Battle Creek.

Society News.—Dr. Frederick H. Cole, Detroit, discussed "Obstruction of the Vesical Neck" before the county medical society in St. Clair November 16.——Dr. Owen H. Wangensteen, Minneapolis, addressed the surgical section of the Wayne County Medical Society November 29 on "Suction in the Treatment of Intestinal Obstruction."——Dr. Harold L. Morris, Detroit, discussed "Cancer of the Bladder" before the county medical society in Jackson, November 16.——Dr. William C. MacCarty, Rochester, Minn., discussed breast tumors before the Ingham County Medical Society, Lansing, November 16.

The Novy Fellowship Fund.—At a meeting of representatives of the medical classes of the University of Michigan, it was decided on behalf of the alumni of the medical school to initiate a ten year campaign for the endowment of a Frederick G. Novy Fellowship Fund for Research in Bacteriology. Dr. Novy joined the university in 1886 as assistant in organic chemistry. He became dean emeritus and professor emeritus of bacteriology in 1935. A resolution adopted at the meeting provides that the fund shall be administered by the board of regents of the university, the principal sum to remain intact and disbursements from its earnings to be made on recommendation of the director of the department of bacteriology and the executive committee of the medical school to the president of the university and the board of regents. The fund is to be used only for nonrecurrent research purposes.

MINNESOTA

Annual Registration Due During January.—Every practitioner of medicine and surgery holding a license to practice in Minnesota is required by law to register annually during January, with the secretary of the board of medical examiners, and at that time to pay a fee of $2. A licentiate who practices without renewing his license is guilty of a misdemeanor and is liable to prosecution.

MISSISSIPPI

New Venereal Disease Clinic.—A clinic providing free treatment to indigent persons for venereal diseases was opened in Hattiesburg in October, according to the *Health Officer*. Funds have been supplied by the state board of health and the U. S. Public Health Service through social security appropriations.

Society News.—The Coast Counties Medical Society was recently formed by the amalgamation of the Harrison-Stone-Hancock Counties Medical Society and the Jackson County Medical Society, bringing all the counties in the ninth district into one organization. Dr. Edwin B. Van Ness, Gulfport, is president, and Dr. Daniel L. Hollis, Biloxi, is secretary.—— At a meeting of the Delta Medical Society in Greenwood, October 13, the speakers included Drs. Fred M. Sandifer Jr., Greenwood, on "Varicose Veins"; Eugene R. Nobles, Rosedale, "The Problem of Acute Abdominal Pain"; Hugh A. Gamble, Greenville, "Operative Treatment of Carcinoma of the Breast"; George J. Mancill, Indianola, "Obstetrics in General Practice"; James W. Barkley, Belzoni, "Immunization Against Communicable Diseases," and Gilbert F. Douglas, Birmingham, Ala., "Study of Sterility, Using the Rubin Test."——Speakers before the Clarksdale and Six Counties Medical Society, November 10, included Drs. Claude F. Varner, Memphis, on appendicitis; William P. Warfield, Clarksdale, upper respiratory infections in infants and children, and Charles S. Paddock, Memphis, pyelitis in pregnancy. Drs. William L. Little, Wesson, and Joseph E. Green, Laurel, president and president-elect respectively of the state medical association, also addressed the meeting.

NEBRASKA

Bequest for Cancer Research.—A public school teacher of Omaha recently bequeathed $1,600 to the Creighton University Tumor Clinic at St. Joseph Hospital. According to the *Nebraska State Medical Journal*, this fund will be the nucleus of an endowment fund, the income from which will be for cancer research.

NEW JERSEY

Public Health Meeting.—The sixty-third annual meeting of the New Jersey Health and Sanitary Association was held in Princeton, December 10-11. Among speakers at various sessions were Drs. Russell L. Cecil, New York, on "Methods of Reducing Pneumonia Mortality"; Herbert R. Edwards, New York, "Latent Tuberculosis and Its Significance in the Control Program"; William D. Stroud, Philadelphia, "Heart Disease," and Livingston Farrand, Ithaca, N. Y., "Health Education in Its Broader Aspects."

Society News.—The Society of Surgeons of New Jersey held its twenty-fifth anniversary meeting in Trenton, November 20. In the morning operative clinics were held at the Mercer and St. Francis hospitals. After luncheon at the Stacy-Trent Hotel, the afternoon was devoted to the showing of surgical motion pictures. Dr. Frank G. Scammell, Trenton, president of the society, presided at an anniversary dinner in the evening. Dr. George Blackburne, Newark, was elected president for the coming year and Dr. Walter B. Mount, Montclair, was reelected secretary.

State Board Activities.—Among unlicensed practitioners convicted through activities of the state board of medical examiners in recent months are the following reported in November:

Bash Cruso, who was treating foot ailments in a shoe store in Jersey City.
Percy Ridout, an unlicensed chiropractor of Englewood.
John E. Usher, a licensed chiropractor of Orange, who was practicing electrotherapy.
Israel Shmid, a naturopath of Lakewood; found guilty on a similar charge in 1929.
Nathan H. Fleischner, a registered pharmacist of Englewood.
Paul Piekarsky, a licensed chiropodist of Paterson.
Frank Sanduzzi, a registered pharmacist of Newark.
George Maza, an unlicensed chiropractor of Newark.
James N. Conroy, registered pharmacist of Moorestown.
Nicholas Farmakis, Orange, who gave his patients medicine prepared by himself.

NEW YORK

Medical Building Dedicated.—The new building of the Syracuse University College of Medicine was dedicated November 22 with ceremonies in the auditorium of the building. The speakers were:

Dr. Henry A. Christian, Hersey professor of the theory and practice of physic, Harvard University Medical School, Boston, The Fruition of the Clinician.
Dr. Edward S. Godfrey Jr., state health commissioner, Albany, The Medical School in the Field of Public Health.
Dr. Ray Lyman Wilbur, president of Stanford University, California, and chairman of the Council on Medical Education and Hospitals, American Medical Association, The March of Medicine.

The alumni held their annual reunion in the building November 20 and there was open house for the citizens of Syracuse November 21. The five-story building, financed by a PWA loan of $850,000, was designed in English Georgian style by the late James Russell Pope and Dwight James Baum. Laboratories, classrooms, lecture rooms and departmental offices open off three main corridors on each floor; each department's laboratories, classrooms and offices are adjoining. An auditorium seating 400 is on the first floor at the rear of the building. The college library occupies two floors in one wing. The top floor is devoted to the Hendricks Research Laboratory for research in infant feeding. Ground was broken for

New Medical School Building, and the Syracuse Memorial Hospital.

the new building June 2, 1936, and President Franklin D. Roosevelt laid the cornerstone the following September 29. It is the fourth unit in a plan for a medical center initiated by the college in 1925. Previously completed are the Syracuse Memorial Hospital, shown at the right of the photograph, the State Psychopathic Hospital and the city communicable disease hospital.

New York City

Foundation Opens New Departments.—The Hecksher Foundation for Children, with headquarters at Fifth Avenue and One Hundred and Fourth Street, announces establishment of a department of hygiene and preventive medicine under the direction of Dr. Heinz R. Landmann. It has also opened a child guidance clinic under the direction of Jacob S. List, Ph.D., a psychologist. Dr. Landmann graduated from the University of Bern, Switzerland, in 1934 and was licensed in 1935. The Hecksher Foundation for Children was established in 1921 by August Hecksher.

Promotions at New York University.—Dr. Karl M. Bowman was recently promoted from professor of clinical psychiatry to professor of psychiatry to succeed Dr. Menas S. Gregory, now professor emeritus, at the New York University College of Medicine. Dr. Joseph Edward Connery has been promoted to be professor of clinical pathology to succeed the late Dr. Arthur R. Mandel, and Dr. Clarence E. de la Chapelle is acting chairman of the department of medicine. Other promotions are: Drs. Emery A. Rovenstine, to be professor of anesthesia in the department of surgery; Lauretta Bender, clinical professor of psychiatry; Frank J. Curran, assistant clinical professor of psychiatry, and Joseph Goldstein, assistant clinical professor of pediatrics.

Medal to Honor Dr. Snow.—At a dinner in honor of Dr. William F. Snow, managing director of the American Social Hygiene Association, October 1, at the Waldorf-Astoria, Dr. Snow was presented with a bronze medallion portrait of himself. It is planned to strike a medal from the original sculpture and to award it from time to time as the William Freeman Snow Medal for Distinguished Service in Social

Hygiene. A committee of the board of directors of the association will make the awards. Speakers at the dinner were Major-Gen. Merritte W. Ireland, Washington, D. C., who was toastmaster; Dr. Wilbur A. Sawyer; Sir Arthur Newsholme, London; Miss Katharine F. Lenroot, director of the Children's Bureau, Washington, D. C.; Dr. Livingston Farrand, former president of Cornell University; Dr. Thomas Parran, surgeon general, U. S. Public Health Service, Washington, D. C., and Dr. John H. Stokes, Philadelphia. Dr. Edward L. Keyes presented the medal.

NORTH CAROLINA

Correction—Annual Registration of Physicians.—The item in THE JOURNAL last week under North Carolina with respect to the annual registration required of physicians was in error. The item should have appeared under North Dakota. Physicians in North Carolina are not required to register annually.

Sanatorium Dedicated.—A new state sanatorium for tuberculosis, built with PWA assistance at a cost of $625,000 on Black Mountain near Asheville, was dedicated November 11 with an address by Gov. Clyde R. Hoey. Dr. Paul P. McCain is superintendent of the new 165 bed institution; Dr. Samuel M. Bittinger is medical director and associate superintendent. Dr. McCain is also in charge of the state's other public sanatorium, of 480 beds, known as the North Carolina Sanatorium for Treatment of Tuberculosis at Sanatorium, near Raeford in Hoke County, and Dr. Bittinger has been assistant superintendent and associate medical director.

NORTH DAKOTA

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in North Dakota is required by law to register annually on or before January 1, with the secretary-treasurer of the board of medical examiners, and at that time to pay a fee of $5 if a resident of North Dakota, or $2 if a nonresident. A practitioner may not lawfully practice if he has not registered. If he does so his license may be revoked and can be reinstated on the payment of unpaid fees and 50 cents for each month of default.

OKLAHOMA

Society News.—At the annual joint meeting of the Garfield County Medical Society and the Northwestern District Dental Society in Enid, November 18, the speakers were Charles R. Lawrence, D.D.S., Enid, on "The Relations of the Dentist and the Physician in Care of the Patient" and Dr. James D. Osborn Jr., Frederick, secretary of the state board of medical examiners, who discussed an initiative bill proposing to change the composition of the state board.

PENNSYLVANIA

Society News.—Dr. Bertram M. Bernheim, Baltimore, addressed the York County Medical Society, York, November 20, on "Diagnosis and Treatment of Peripheral Vascular Disease."——Drs. John B. Nutt and Thomas Marshall West addressed the Lycoming County Medical Society, Williamsport, December 10, on "Toxemias of Pregnancy" and "Treatment of Bladder Tumors" respectively.——Dr. Othello S. Kough, Uniontown, gave an address and demonstration on "Artificial Pneumothorax in the Treatment of Tuberculosis" before the Fayette County Medical Society, Uniontown, December 2.——At the annual dinner of the Cambria County Medical Society, Johnstown, December 9, Judge John H. McCann, Ebensburg, spoke on "The Doctor and the Law" and Dr. Olin G. A. Barker, Johnstown, showed motion pictures "Through Africa from Cairo to Capetown."——The Harrisburg Academy of Medicine has purchased a larger building for its headquarters.

Philadelphia

Personal.—Members of the Proctologic Society of the Graduate Hospital gave a dinner November 20 in honor of Dr. Collier Ford Martin, professor and vice dean of proctology, University of Pennsylvania Graduate School of Medicine. The speakers included Drs. William Wayne Babcock, Edwin S. Cooke and Wilmer Krusen, Philadelphia; Clement L. Martin, Chicago; Descum C. McKenney, Buffalo; Frank C. Yeomans, New York, and Emmett H. Terrell, Richmond, Va. Dr. Harry E. Bacon, Philadelphia, was chairman.

Dean Charles H. LaWall Dies.—Charles Herbert LaWall, Pharm.D., dean of pharmacy in the Philadelphia College of Pharmacy and Science, died of pneumonia December 7 in the Jewish Hospital, aged 66. Dr. LaWall graduated from the Philadelphia College of Pharmacy in 1893. In 1900 he was appointed instructor at his alma mater. In 1906 he was made associate professor of the theory and practice of pharmacy and in 1918 succeeded Joseph P. Remington as dean. For many years Dr. LaWall was chemist for the bureau of foods and chemistry of the Pennsylvania Department of Agriculture and the Pennsylvania Board of Pharmacy. He was elected to the revision committee of the U. S. Pharmacopeia in 1910 and served continuously on subsequent committees, including two years as chairman. He was also associated with the revision committees of the National Formulary and the U. S. Dispensatory. Among honors conferred on Dr. LaWall were the Remington Medal of the American Pharmaceutical Association and honorary degrees from the University of Pittsburgh and Susquehanna University. He was president of the American Pharmaceutical Association in 1919 and the American Association of Colleges of Pharmacy in 1923. During the World War he was a member of the auxiliary committee on drugs and medicine of the War Industries Board. Dr. LaWall was also co-editor of the seventh and eighth editions of Remington's "Practice of Pharmacy."

WEST VIRGINIA

Society News.—Dr. Walter N. Rowley, Huntington, addressed the Fayette County Medical Society, Montgomery, November 9, on "Estrogenic and Gonadotropic Hormone Therapy."——Dr. William F. Rienhoff Jr., Baltimore, addressed the Harrison County Medical Society, Clarksburg, November 4, on diseases of the gallbladder and gall ducts. Dr. William F. Snow, New York, spoke briefly on the syphilis campaign. ——Dr. Amos H. Stevens, Fairmont, addressed the Monongalia County Medical Society, Morgantown, November 2, on "Prognosis and Late Manifestations of Rheumatic Heart Disease."

New Quarters for Radiologic Clinic.—The Huntington Radium and X-Ray Clinic opened new quarters in the Memorial Hospital, Huntington, November 11, with public inspection in the afternoon and a dinner meeting of the Cabell County Medical Society in the evening. Dr. Edwin A. Merritt, Washington, D. C., gave an address on "Preoperative Radiation as a Therapeutic and Diagnostic Measure," which was discussed by Dr. Henry Schmitz, Chicago. The clinic now has a high voltage therapy x-ray machine of 220,000 volts. Dr. James Edward Hubbard is director and Dr. Walter Beckett Martin is associate director of the clinic, which was founded in 1921.

GENERAL

Meeting of Psychoanalytic Association.—The thirty-ninth meeting of the American Psychoanalytic Association will be held in Washington, D. C., December 27-28, with headquarters at the Hotel Shoreham. Among the speakers will be:

Dr. Sandor Rado, New York, Etiology and Treatment of the Neuroses.
Dr. Felix Deutsch, Boston, Pain as a Psychosomatic Problem.
Dr. Lucia E. Tower, Chicago, Premature Birth as a Factor in Development of a Paranoid Depressive-Mechanism.
Dr. Helen Flanders Dunbar, New York, Psychoanalysis and the General Hospital.

Bequests and Donations.—The following bequests and donations have recently been announced:

Mount Sinai Hospital, New York, $10,000 by the will of Mrs. Carrie L. Lehman.
Hospital for Joint Diseases and Montefiore Hospital, New York, $2,000 each by the will of Samuel Frank.
Sinai Hospital, Baltimore, $10,000 and his medical library, by the will of the late Dr. Harry Adler.
Presbyterian Hospital, New York, $10,000 by the will of Henry T. Sloane.
Germantown Dispensary and Hospital, Germantown, Pa., $5,000 by the will of the late Jane Harmer, at the termination of a trust.

Meeting of Medical Students.—The fifth annual convention of the Association of Medical Students will be held at the medical schools of the University of Chicago and the University of Illinois December 29-31. Addresses of welcome will be delivered by Drs. Basil C. H. Harvey, dean of medical students, Division of Biological Sciences, University of Chicago; David J. Davis, dean, University of Illinois College of Medicine, and Olin West, Secretary and General Manager, American Medical Association. Panel discussions, lectures and clinics will make up the program. Special features will include tours of the medical schools and the Headquarters of the American Medical Association.

Special Board Examination.—The American Board of Obstetrics and Gynecology announces that the next examination for group B candidates who have filed applications will be held in various cities of the United States and Canada Feb. 5, 1938. This is the written examination and review of case histories. The general oral clinical and pathologic examinations for all candidates (groups A and B) will be conducted by the entire board in San Francisco, June 13-14, immediately before the annual session of the American Medical Association.

Applications for admission to the June 1938 group A examinations must be on an official application form and must be filed with the secretary before April 1, 1938. For further information and application blanks address Dr. Paul Titus, secretary, 1015 Highland Building, Pittsburgh.

Biography of Reginald H. Fitz.—Dr. Hyman Morrison, clinical professor of medicine, Tufts College Medical School, Boston, is gathering material for a biography of Reginald Heber Fitz (1843-1913) and requests the assistance of THE JOURNAL in reaching readers who knew Dr. Fitz personally or who may have some of his correspondence. Dr. Morrison writes that he will be responsible for the safe return of any letters sent to him. Dr. Fitz graduated at Harvard University Medical School in 1864 and spent several years in European centers. He returned in 1870 and joined the faculty at Harvard. He was active in the affairs of the school and his clinical work produced important results. In 1886 he published the article in which he established the importance of perforation of the appendix. He retired from Harvard in 1908 as professor of medicine and died Sept. 30, 1913.

Society News.—Dr. Robert Tait McKenzie, Philadelphia, was elected president of the Academy of Physical Medicine at its annual meeting in Philadelphia in October. Drs. Rolland A. Case, Cleveland, and William H. Schmidt, Philadelphia, were elected vice presidents and Dr. Herman A. Osgood, Boston, secretary. The next annual session will be in Washington, D. C.——Dr. James W. Jervey, Greenville, S. C., was elected president of the Southern Medical Association at its annual meeting in New Orleans November 30-December 3, and Drs. Lucien A. Le Doux, New Orleans, and Lee Rice, San Antonio, Texas, were elected vice presidents. The next meeting will be held in Oklahoma City.——A meeting of the secretaries of the sections of the American Association for the Advancement of Science and those of the affiliated societies will be held at the Claypool Hotel Friday, December 31, during the annual session of the association.

Western Surgical Association.—Dr. Casper F. Hegner, Denver, was elected president of the Western Surgical Association at its annual meeting in Indianapolis, December 3-4. Drs. Charles L. Patton, Springfield, Ill., and Verne C. Hunt, Los Angeles, were elected vice presidents and Dr. Albert H. Montgomery, Chicago, was reelected secretary. The 1938 convention will be in Omaha. Among speakers on the program were:

Dr. John Alexander, Ann Arbor, Mich., The Indications, Technic and Results of Surgery for Bronchiectasis.
Dr. Angus L. Cameron, Minot, N. D., Primary Malignancy of the Jejunum and Ileum.
Dr. Charles W. Mayo, Rochester, Minn., A New Method of Repair of Complete Rectal Prolapse.
Dr. Fred F. Attix, Lewistown, Mont., Purulent Pericarditis Due to the Pneumococcus.
Dr. Edgar L. Gilcreest, San Francisco, Lesions of the Shoulder.
Dr. Kellogg Speed, Chicago, Spondylolisthesis.
Dr. Claude J. Hunt, Kansas City, Mo., Pancreatic Cyst.
Dr. Gordon S. Fahrni, Winnipeg, Manit., Hyperparathyroidism.

Pan American Cruise Congress.—The seventh cruise congress of the Pan American Medical Association will leave New York January 15 and return January 31. Among speakers from the United States will be:

Dr. William D. Haggard, Nashville, Technic in Treatment of Fibroid Tumors.
Drs. Chevalier Jackson and Chevalier L. Jackson, Philadelphia, Cancer of the Larynx.
Dr. Edwin C. Ernst, St. Louis, Recent Developments in Relation to the Radiation Management of Cancer.
Dr. Webb W. Weeks, New York, Operation for Chronic Simple Glaucoma.
Dr. Howard R. Hartman, Rochester, Minn., Treatment of Hemorrhagic Ulcer of Stomach or Duodenum.
Dr. Henry D. Furniss, New York, Urinary Incontinence in Women.
Dr. Joseph J Eller, New York, Cosmetic Results in Treatment of Skin Tumors.
Dr. James Ewing, New York, Cancer Pathology.
Dr. Jerome Webster, New York, Plastic Surgery Technic.
Dr. Herman N. Bundesen, Chicago, Amebiasis.
Dr. Lee M. Hurd, New York, Sinus Operations.
Dr. Fred H. Albee, New York, Surgical Restoration of Motion in Bony, Stiff Joints.

Among other speakers will be Dr. Jose Arcé, Buenos Aires, Argentina, on "Twenty Years in Chest Surgery."

Academy of Orthopaedic Surgeons.—The sixth annual meeting of the American Academy of Orthopaedic Surgeons will be held at the Hotel Biltmore, Los Angeles, January 17-20, under the presidency of Dr. Arthur Bruce Gill, Philadelphia. Registration will begin Sunday afternoon at 2 o'clock, January 16. A special train on the Atchison, Topeka and Santa Fe Railroad will leave Chicago January 10 at 10:15 a. m. There will be a clinical demonstration Monday morning January 17 and scientific sessions will begin in the afternoon. There will be symposiums on nonunion and bone grafts, fractures of the spine, and manipulative surgery. Among the speakers on the program will be Drs. Norman T. Kirk and Howard C. Naffziger, San Francisco; Willis C. Campbell, Memphis, Tenn.; Melvin S. Henderson, Rochester, Minn.; Edwin W. Ryerson, Chicago; George E. Bennett, Baltimore; William B. Carrell, Dallas, Texas; Arthur G. Davis, Erie, Pa.; William V. Cone and William George Turner, Montreal; Philip D. Wilson, New York; Johan H. Waldenström, Stockholm, Sweden, and H. Watson Jones, Liverpool, England.

Symposium on Syphilis.—Section N, the Medical Sciences, of the American Association for the Advancement of Science will devote its entire program at the meeting, December 27-January 1, to a symposium of twenty-nine papers on syphilis. The papers are grouped in sessions on the following topics: historical; the causative agent; closely related agents, immunity, pathology; various forms of the disease; diagnostic aids; treatment, chemotherapy and toxicity of drugs. Among the speakers will be:

Dr. William Allen Pusey, Chicago, The American Origin of Syphilis.
Dr. Norman R. Ingraham Jr., Philadelphia, Spirochaeta Pallida and the Etiology of Syphilis.
Dr. John A. Kolmer, Philadelphia, Serologic Reactions in Relation to Infection and Treatment of Syphilis.
Dr. Paul A. O'Leary, Rochester, Minn., Neurosyphilis.
Dr. Charles C. Dennie, Kansas City, Mo., Congenital Syphilis.
Reuben L. Kahn, Sc.D., Ann Arbor, Mich., The Outstanding Features of the Kahn Antigen.
Dr. Benjamin S. Kline, Cleveland, The Outstanding Features of the Kline Antigen.
Dr. Walter M. Simpson, Dayton, Ohio, High Temperatures.
Dr. Harry Eagle, Baltimore, The Direct Spirochetostatic and Spirochetocidal Action of the Arsphenamines.
Dr. Dudley C. Smith, University, Va., Untoward Reactions—Intercurrent Infections.

Dr. Thomas Parran, surgeon general, U. S. Public Health Service, Washington, D. C., will address a general session of the association on "Syphilis: A Public Health Program."

Medical Bills in Congress.—*Bills Introduced:* S. 3098, introduced by Senator Capper, Kansas, proposes to provide for uniform regulation of marriage and divorce. The bill provides, among other things, that no license to marry shall be issued to a person who is insane or an imbecile, pauper, epileptic, feebleminded or afflicted with tuberculosis or a venereal disease. S. 3120, introduced by Senator Walsh, Massachusetts, proposes to authorize the President to appoint for temporary service in the Navy 100 acting assistant surgeons, who shall have the rank and compensation of assistant surgeons. H. Res. 375, submitted (by request) by Representative Stack, Pennsylvania, proposes to provide "That all World War veterans' service records become an official part of their medical record, so that the Veterans' Administration must consider any ailment, from which a veteran may be suffering, not proven as service-connected by his medical record, to be established as service-connected by consideration of his service record." H. R. 8655, introduced by Representative Dunn, Pennsylvania, proposes to authorize an appropriation of $200,000,000 for the prevention and cure of cancer, infantile paralysis, tuberculosis, blindness, deafness and "other social diseases." H. R. 8641, introduced by Representative Palmisano, Maryland, proposes to provide that any honorably discharged ex-service man who entered the service prior to Nov. 11, 1918, and served ninety days or more during the World War, and who is or may hereafter be suffering from a 25 per centum or more permanent disability, not the result of his own wilful misconduct, which was not acquired in the service during the war, or for which compensation is not payable, shall be entitled to receive a disability allowance at prescribed rates.

CANADA

North Pacific Surgical Association.—The annual meeting of the North Pacific Surgical Association was held in Vancouver, B. C., November 18-20, with Dr. William E. Gallie, professor of surgery, University of Toronto Faculty of Medicine, Toronto, as the guest speaker. Dr. Andrew A. Matthews, Spokane, Wash., was elected president; Drs. Gordon C. Kenning, Victoria, B. C., and Robert D. Forbes, Seattle, were elected vice presidents and Karl H. Martzloff, Portland, Ore., is secretary.

Orthopedic Service for Paralysis Victims.—The department of health of Saskatchewan has established a special orthopedic service at the Grey Nuns' Hospital, Regina, for treatment of residual paralysis arising out of a recent outbreak of poliomyelitis. The plan includes three weeks of treatment with medical and hospital care and transportation paid and special splints gratis. It is also a part of the plan to have the child's mother or some responsible person spend three days at the hospital for instruction in continuing the treatment at home. It was estimated that out of 445 cases of poliomyelitis there would be at least 100 patients requiring treatment.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 20, 1937.

The Annual Health Report

In his annual report, just published, Sir Arthur MacNalty, chief medical officer of the Ministry of Health, compares the vital statistics of today with those of a century ago. In 1936 the crude death rate was 12.1 per thousand against 22.4 in the eighteen forties, the infant mortality 59 per thousand live births against 153. The number of infants who died under 1 year of age, 35,425, was less than half the number who would have died under the conditions as recent as thirty years ago. The death rates for both respiratory and nonrespiratory tuberculosis were in 1936 the lowest on record. The standardized death rate from all forms of tuberculosis was 657 per million, against 3,476 in the fifties of the last century. It is noted as "particularly satisfactory" that the mortality from tuberculosis among young women, which showed some increase, is again declining and at an increasing pace.

In 1936 the birth rate was 14.8, a slight increase on the 14.7 of 1935 and 0.4 above that for 1933, which was the lowest on record. The five principal causes of death remain the same as for many years and in the same order: (1) diseases of the heart and circulatory system, (2) cancer, (3) respiratory diseases, (4) diseases of the nervous system and (5) tuberculosis. But between the ages of 15 and 65 tuberculosis takes the third place and diseases of the nervous system the fifth. The proportion of deaths from heart and circulatory diseases has steadily risen during the past five years. During the same period the proportion of deaths from tuberculosis has steadily fallen; the cancer mortality has risen.

It was claimed not long ago that typhoid had practically vanished from this country, because of improved sanitation, but a serious increase has recently taken place. In 1936 there were 2,490 notifications (including paratyphoid) with 257 deaths. In 1935 the corresponding figures were 1,750 and 174. At present a serious outbreak is in progress in Croydon, a town near London. It has been traced to a contaminated well supplying drinking water. Eighteen new cases have been reported today, bringing the total up to 137, with six deaths. The disease has appeared also in London.

The maternal mortality in 1936 was 3.65, a slight reduction from 3.94 for 1935, which again was a reduction from 4.41 for 1934. Puerperal sepsis accounted for 1.34, leaving 2.31 for other causes. Abortion, which appears to be frequent and increasing, is responsible for a number of deaths from puerperal sepsis.

A section of the report is devoted to poisoning from lipsticks and other cosmetics. It is pointed out that it is desirable to determine the ingredient to which the patient is sensitive, since a formula without the offending ingredient enables the application to be resumed with impunity. The dye is mostly at fault, and that most frequently incriminated is eosin. Hair dyes of vegetable origin seem to be innocuous, but those which depend on paraphenylenediamine or its derivatives might give rise in susceptible persons to severe dermatitis of the scalp, with other developments, and fatalities have been recorded. Eyelash stains containing para dyes might also cause trouble; face lotions and powders are capable of causing dermatitis in certain circumstances.

Response to the Fitness Campaign

The British national effort to develop recreative physical training has aroused widespread interest at home and abroad. The Central Council of Recreative Physical Training has received many inquiries from other countries, and information of an advisory nature has been sent by request to Australia, Austria, Belgium, Burma, Canada, Ceylon, Denmark, Egypt, France, Germany, India, Italy, Jamaica, Kenya, Lithuania, New Zealand, Poland, Rumania, South Africa, Sweden, Switzerland and the United States. The national register of leaders in Britain now includes about 3,000 names. To meet the immediate need in the training and provision of leaders, short courses have been held in the evenings or week ends or during vacations. Half-day training courses have proved of great value. This concentrated form of instruction not only gives already trained teachers new material but also arouses enthusiasm. The council considers that 1937 will stand out as the year of national awakening to the urgency of universal physical recreation. This it attributes largely to the work of those individuals and organizations who have labored untiringly toward that end for many years and to further whose efforts the Central Council has offered the strength of coordinated action. Influences from many foreign countries have also been at work and a splendid press campaign has set the seal on success. "Complete fitness in the individual," the report says, "is unfortunately rare. Too often physical and mental well-being are betrayed by moral laxness, or there is mental strength with bodily disability, or else physical and moral health is accompanied by weak mentality. The aim must always be toward the highest, which is perfect ability in every sphere—fitness for life, not merely fitness for games. Such a comprehensive conception presupposes full observance of enlightened rules of nutrition and hygiene."

The Government and Precautions Against Air Raids

The local authorities have objected to bearing so much of the cost of the precautions to protect the civilian population against air raids. The government has therefore undertaken the greater part of the cost. In a memorandum it points out that it has already assumed a substantial liability in the supply of respirators for the whole civilian population, the maintenance of anti-gas training schools, the supply of bleaching powder for decontamination and the provision of protective clothing for the air raid services. It now proposes to pay the whole cost of most of the material and equipment for these. It proposes to ask the local authorities to assume a share of the responsibility only in those matters in which they will administer. The government will make grants to an extent varying from 60 to 75 per cent of the expenditure of the local authorities on air raid precautions. These include the repairing of streets damaged by air raids, the control of lights, decontamination work and fire fighting. The government will provide such fire fighting apparatus as may be necessary for emergency purposes. It will also provide stretchers, blankets, the equipment needed for decontamination and rescue parties, and the equipment and stores for first aid posts and casualty clearing hospitals. On the other hand, the local authorities will undertake the services for which provision cannot be made centrally: structural precautions in public buildings, the provision of public refuges, the organization of local services, training of personnel for decontamination, emergency fire fighting, rescue and repair work, and the provision of first aid.

The Aborigines of Australia

It has long been thought that, like the Tasmanians, the Australian aborigines will not survive the coming of the white man. Recently some 1,800 sent a petition to the king asking him to save them from extinction and empower one of their own people or a sympathetic white inhabitant to represent them in the federal parliament. The causes of their decline are various. The occupation by the white colonists of land over which the natives once hunted and roamed freely has led to detribalization. They have taken to living in squalid camps on the fringes of bush or cattle stations, where they lose interest in life and contract the diseases of the white man. Many will not accept the medical help provided by the government and run in panic

at the mention of the "doctor man," whose work they regard as a kind of sorcery. An alarming fact recently discovered by anthropologists is that tribes which have not been disturbed in the remote parts of the continent are restlessly moving off their traditional lands and that some of them are drifting into areas of white settlement, where their fate seems only too certain. Prof. F. Wood Jones, the anatomist and anthropologist, who has vacated his chair at Melbourne University for one at Manchester, made a scathing indictment of Australia's neglect of her aborigines in his farewell address to the Victorian Anthropological Society. He said that when the white colonists arrived in 1788 there were 300,000 aborigines living healthily and happily. Today there were 50,000, with many half castes, who were existing miserably. The dole had pampered natives already degraded. There should be a central anthropologic administration of the natives with medical attention and better social conditions. The government has not entirely neglected the native problem, as Prof. Wood Jones seems to imply, and has supplied both grants and medical attention, but the help has not been sufficient.

PARIS

(From Our Regular Correspondent)

Nov. 20, 1937.

The Annual Congress of Urologists

The thirty-seventh annual congress of the French Urologic Association was held October 4-9 at the Paris Medical School under the presidency of Dr. Lepoutre of Lille. As is customary in France, one or more subjects are chosen by vote of the members at the previous year's meeting. One or two members are then appointed by the president to prepare a complete analysis of the literature of the respective subject, including personal observations. This report is sent to each member in printed form about a month before the following year's meeting, so that those who take part in the discussion can be prepared. The subject chosen for the 1938 congress is evaluation of transurethral resection, and for the 1939 congress the treatment of malignant neoplasms of the kidney. The subject chosen for this year was the surgical treatment of nephritis.

This report was read by Drs. Chabanier, Gaume and Lobo-Onell, who constitute the medical and urologic members of a team especially interested in developing the surgical aspects of medical nephropathies, as they are termed here; viz., of nephritis and hypertension. Failure of medical treatment to check the progress of the renal changes appeared to Harrison and Edebohls to be an indication for operative intervention. The lack of an adequate classification and reliable functional tests soon led to discarding surgery until recently, when renewed interest has been shown. In addition to nephrotomy and decapsulation, other procedures such as denervation, adrenalectomy and splanchnicotomy have been employed to relieve hypertension. The report was based largely on an analysis of 117 personal observations. The first question that presented itself at the onset of their work was to find a classification. That of Widal, which was based on the functional syndromes, did not appear as satistactory as that of Volhard and Fahr, which the authors of the report have had occasion to verify by biopsy in 250 cases of different types of nephritis.

According to Volhard and Fahr, there are four principal types of nephritis: (*a*) glomerulonephritis, (*b*) the nephroses, (*c*) the nephro-angioscleroses and (*d*) interstitial nephritis of infectious origin. There are two groups under the heading glomerulonephritis, one in which the changes are diffuse and another in which they are focal. Both of these are most frequently secondary to buccopharyngeal infections. In the acute diffuse form, the clinical picture is that of a slight edema, hematuria, slight rise of blood pressure, moderate albuminuria and casts, lasting from fifteen to twenty days. Volhard believes that the condition persists in 30 per cent, but the authors found this to be true of a far greater number of cases. In the chronic diffuse form, decapsulation has been followed by marked improvement in the hematuria, in pain and in lessening the frequency of acute exacerbations so frequently observed in this group. The salient feature of focal glomerulonephritis is hematuria due to degenerative glomerular lesions. Uncomplicated cases in this group had not been seen by the authors, and the value of operation in cases reported as "néphrites hématuriques" was open to doubt as long as they had not been checked by microscopic study.

In the second principal Volhard and Fahr type, which includes the nephroses and amyloses, decapsulation has been successful in only a few cases of mercurial origin. This is true also in an occasional case of lipoid nephroses.

In the nephro-angiosclerosis type there are two groups, a benign one in which the hypertension is the only symptom corresponding to sclerotic changes in the renal arteries and a malignant form or hypertension associated with rapidly progressive involvement of renal function and endarteritis. Denervation performed by the authors in forty cases was followed by a drop in blood pressure, often quite marked, but which was of only a few months duration. There is, however, a striking improvement in the general condition of the patient and an appreciable interval in the evolution of the disease. In forty-five published adrenalectomies, to which the authors added two personal observations, the operation seems to have been followed by improvement similar to that noted after denervation. In the absence, however, of any microscopic evidence in the majority of the reported cases, it is difficult to decide as to the nature of the underlying pathologic lesions. Preference is to be given to denervation except in cases of adrenal tumor.

In the fourth Volhard and Fahr type, the nonsuppurative infectious type of interstitial nephritis, no typical clinical picture is found except in the cases in which an oliguria or anuria corresponds to edema and round cell infiltration in the renal interstitial tissue. Eleven personal cases of secretory anuria, verified by finding edema in the biopsy specimens, were reported. In all the cases, although there was a marked temporary increase in the output of urine, only two patients recovered. They found twenty-three reports of secretory anuria of varying etiology without microscopic control in which recovery followed either decapsulation or nephrotomy. Intervention is indicated if the anuria is of more than three days' duration and should be combined with medical treatment. The conclusions of Volhard and Fahr are that operative intervention yields results in medical nephritis which are beyond all doubt, even in cases in which little can be expected of such treatment. The control of all surgical cases ought to be made by microscopic examinations of sections of tissue removed at operation. If surgery is to be of any help, one must not wait too long before employing it. The discussion was opened by Professor Chevassu of Paris, who doubted the value of biopsy because of the fragility of the convoluted tubules. He emphasized the necessity of a cytobacteriologic examination of the urine in nephritis. If there is a marked increase in the number of leukocytes, a diagnosis of an infectious origin must be made, but there were many cases of infectious nephritis in which as few leukocytes are found as in the suppurative hematogenous cortical form. Cases of nephritis of apparently infectious character call for treatment of the upper respiratory tract by specialists, because the primary focus is in the nasopharynx and, unless such a focus is eliminated, the nephritis will not improve.

Le Clerc Dandoy of Brussels maintained that abnormal mobility of the kidney plays an important part in essential hematuria or "néphrite hématurique." Orthostatic albuminuria is often due to the passive hyperemia in movable kidney.

Louis Michon of Paris based his conclusions on thirty personal observations. At the onset of an acute glomerulonephritis, decapsulation often improves and in some cases will cure the condition. In anuria due to acute glomerulonephritis, early

bilateral decapsulation is to be recommended. Even in acute mercurial nephrosis, decapsulation in conjunction with the administration of saline solution and sodium bicarbonate solution aids in increasing diuresis. He had never observed any benefit from decapsulation in acute exacerbations of the chronic types of nephritis. Denervation is a much simpler method of treatment of hypertension than adrenalectomy or splanchnectomy and equally efficacious. The immediate result is satisfactory, but it has not proved to be permanent in a single case. Perhaps the end results would be better if such cases came to operation earlier.

Darget of Bordeaux stated that the three indications for operative intervention in chronic nephropathies were (1) anuria and oliguria, (2) hematuria and (3) hypertension. There is no difference of opinion as to the value of decapsulation in acute glomerulonephritis and in interstitial nephritis. In hematurias it is advisable to give transfusions before a decapsulation. Denervation in two sittings is indicated for cases of nephroangiosclerosis. At the same time, the adrenal should be examined for marked pathologic changes calling for adrenalectomy.

Other papers read at this year's urologic congress which were of special interest included the following:

Chevassu of France recommended the use of retrograde ureteropyelography as a check on functional tests and cytobacteriologic examination of the urine in determining the functional capacity of a kidney before operation. He based his opinion on 7,000 cases, having found that, when there was a difference in the function tests between the two kidneys, retrograde ureteropyelography always yielded information as to which was the diseased side and the character of the lesion. Excretory urography had proved to be of little value in many cases because the visualization was often too indistinct to warrant the drawing of any conclusions.

Dos Santos of Portugal recommended nephrectomy as soon as a diagnosis of infarction of the kidney due to embolism or thrombosis of the renal artery or vein had been made. Too long a delay was likely to favor extension of the thrombosis to the vessels of the opposite kidney.

Professor Tiffeneau Appointed Dean of Medical School

At the October 28 meeting of the faculty of the Paris Medical School, the pharmacologist Prof. Marc Tiffeneau was elected as the successor of Professor Roussy, the former dean, who has recently been promoted to the presidency of the University of Paris, better known to foreigners as the Sorbonne. Professor Tiffeneau became a member of the faculty of the medical school in 1910, being appointed at that time associate professor of pharmacodynamics and later occupying the chair of pharmacology. Professor Tiffeneau has an international reputation as an authority on the problem of the relations of chemical composition and pharmacodynamic action, which study has led to the discovery of new pharmaceutical preparations. He has lectured in many foreign countries and is a member of several commissions of the League of Nations, one for the biologic evaluation of drugs and others for the control of opium consumption. He has also been a fellow of the Academy of Medicine since 1927.

Tuberculin Skin Reactions in Girls

At the June 12 meeting of the Paris Tuberculosis Society, Rist and Tuchila said that an investigation among students between the ages of 20 and 22 years had given the following results: At the Montrouge School for Nurses, 27 per cent of 111 pupil nurses had a negative reaction. At the Social Service School this was true of 27 per cent of 111 students, and at the Sèvres Normal School of thirty-three of the students between the ages of 19 to 23 years. In the discussion, Courcoux reported a similar examination of a larger number of pupil nurses and medical students. Among the former, the percentage of negative reactions varied from 29 to 30 and among the medical students it was 33. In closing, Etienne Bernard insisted that a long rest period should be granted every pupil nurse who had a negative skin reaction. This was also the opinion of the phthisiologist Rist.

VIENNA

(From Our Regular Correspondent)

Oct. 15, 1937.

Annual Report on Sickness Insurance

The annual report for 1936 on the various sickness insurance organizations of Austria contains many instructive data. The Workers' Sickness Insurance Club of Vienna, for example, includes among its membership 317,000 directly insured workers and 236,000 relatives of the insured, a total of 553,000 persons. The sum of 4,560,000 Austrian shillings was expended for sick benefits to the directly insured workers and 610,000 shillings for benefits to workers' relatives. These benefits included both general and special medical services. If to the foregoing sums is added the 1,150,000 shillings disbursed for dental care, the grand total amounts to 6,300,000 shillings (more than $1,200,000) or 19.5 per cent of the club's entire income.

The second largest sickness insurance club, that of the federal employees, has a membership of 350,000, with 217,000 in Vienna alone. The ratio of direct insured members within this group to the insured's relatives is 53 per cent to 47 per cent. Expenditures for medical care (general and special) amounted to 7,250,000 shillings (around $1,500,000) or 32 per cent of all funds disbursed by the club. Another 2,500,000 shillings ($500,000) or 11 per cent of all disbursements went for dental care. Therapeutic substances and appliances requisitioned by its members cost the club 2,750,000 shillings, or 13 per cent of expenditures; 21 per cent of the club's income was paid to general practitioners, more than 12 per cent for dental care. In comparison with former years an increase in the number of claims for services of specializing physicians as distinguished from general practitioners has been discernible. The expenditure for pharmaceutic substances and so on was less than 3,000,000 shillings, in contrast to 3,500,000 shillings in the preceding year. Nearly 4,500,000 shillings was spent on hospital care for members. The 1936 statistics show an obvious diminution in the costs of sickness when compared with the figures for previous years. The explanation for this must lie in a generally more favorable condition of health among club members. Already the membership is being drawn from better social strata.

Another similarly organized sickness insurance club is composed of municipal employees of Vienna. It numbers 76,000 directly insured persons and their dependents. In 1936 this club spent 2,000,000 shillings for medical care; namely, 37 per cent of all its disbursements. It is interesting to compare the amounts expended by this club for general and for special medical care. In 1936 there was an average per claimant of 3.69 office calls on and 1.56 house visits from the general practitioners, as against 1.03 office calls on and 0.15 visits from the specialist. A member might choose from among approximately 2,500 general practitioners and 700 specialists. The report also includes analogous data on various minor sick insurance organizations in Vienna. Among the groups represented in the minor clubs are apprentices, assistants and other workers in agriculture, in the butcher trade and in hotels and similar small corporations. The average expenditure of these clubs is fairly constant, amounting to from 18 to 20 per cent of the annual income. Naturally the compensation of the physician who serves one of these minor clubs will be commensurately smaller. The income per physician from this type of practice scarcely averages more than 50 or 60 shillings monthly, as against the average monthly incomes of from 300 to 400 shillings enjoyed by the doctors attached to the larger insurance clubs. There are, however, a fairly large number of so-called upper bracket men

who are able to realize more substantial incomes from practice among the minor clubs. Many specialists in particular (such as surgeons, orthopedists and laryngologists) have been able to earn 2,000 shillings a month, but this has been possible only during the last two years, since the physicians' honorariums in the insurance practice have been based on individual services. The present system works out quite favorably for the attending physician in particular cases.

The Fight Against Disease

Not long ago the new director of Vienna University's Institute of Hygiene, Prof. Dr. Max Eugling, who has been appointed to succeed the hygienist Professor Grassberger, delivered an inaugural address which had as its theme the fight against disease throughout the ages. Professor Eugling indicated that systematic care of the body (hygiene) is the best weapon with which to combat disease and that this fact was known to the ancient Greeks. In Rome, six centuries before Christ, the first regularly planned drainage system was constructed and the public baths would accommodate 5,000 visitors. With the destruction of the Roman Empire in the West by the Germanic invaders the institution of the public baths fell into disuse. The Crusades brought into Europe from the Orient a formidable dissemination of contagious diseases, of which leprosy and bubonic plague are examples. At the close of the fourteenth century there were in France alone some 1,500 leprosariums. Even today there are 1,500,000 lepers among the world's population. But this formerly incurable disease can now be quite favorably influenced by treatment with preparations of chaulmoogra oil. Bubonic plague has an interesting history. It was always endemic in the Orient and is frequently mentioned in the Bible. Effective defenses against the plague were unknown. The closer contact between Europe and the Near East which resulted from the Crusades brought with it frequent opportunities for a dissemination of the contagion. The pest came to assume more and more formidable proportions in Europe. Finally, during the years from 1347 to 1350 western Europe experienced a pandemic of plague (the black death) which took the lives of some 25,000,000 persons, a good third of the entire European population of that time. Thereafter as the pest flared up again and again in particular towns it became customary to boycott and virtually isolate the stricken community, a policy that no doubt prevented a recurrence of catastrophes like the black death. Yet in the course of the last three decades 11,000,000 inhabitants of India have succumbed to the pest. Nowadays excellent results are obtained by a combination of prophylactic procedures such as disinfection of laundry by hot steam, a most reliable measure. Some of the more notable landmarks in the history of the war on disease have been the addition of quinine and the arsenicals to the therapeutic armamentarium against malaria and trypanosomiasis, and the discovery of diphtheria serum by Behring and of arsphenamine by Ehrlich. The introduction of routine antitetanic inoculation of men whose wounds had come in contact with the soil proved a prophylactic measure of tremendous importance during the World War. Throughout the conflict tetanus, once so dreaded in war, remained almost without significance. The best protective inoculation known to man is that against smallpox devised by the English physician Edward Jenner. Smallpox vaccination was first practiced on a large scale in Vienna. It might be added that all types of variola have as good as died out in those European countries in which vaccination is compulsory. The younger generation of doctors in Austria, for example, have never seen a case of genuine smallpox. In conclusion Professor Eugling said that the importance of hygiene cannot be everestimated. Just as formerly the consumption of soap within a country was considered a good indication of that nation's culture or lack of culture, so today the amount of contagious disease within a country may be taken as a similar criterion.

BERLIN

(From Our Regular Correspondent)

Nov. 1, 1937.

Protection Against Diphtheria

The minister of the interior made public, October 2, new guiding principles relative to active protective inoculation against diphtheria. The author states that in the antidiphtheria campaign which has been conducted for many years throughout Germany the procedure that has proved most effective is inoculation. In the future, too, this measure will be relied on whenever an outbreak of diphtheria threatens. However, now as before, voluntary inoculation of large groups of children may be undertaken only with the permission of the ministry of labor. The serum should be injected subcutaneously either into the skin below the clavicle or into the upper part of the arm about on the insertion of the deltoid muscle. No child who has been excused from smallpox vaccination should be submitted to antidiphtheritic inoculation. Dosage should conform to the following prescriptions: If serum that contains 30 protective units per cubic centimeter is used, infants should receive injections of 0.5 cc. and children of school age doses of 0.3 cc. If the serum used contains less than 30 units but more than 10 units per cubic centimeter, infants should receive 1 cc. at each injection, children of school age 0.5 cc. (The dosage should be reduced for debilitated children and children who have already had diphtheria.) To obtain a sufficiently permanent and satisfactory immunization, inoculation with serum of the same strength should be repeated not less than four weeks after the initial injection. If a serum containing from 1 to 10 protective units per cubic centimeter is used, three injections are necessary, each to contain for infants 1 cc. and for children of school age 0.5 cc. The same type of serum ought to be used at all inoculations and the intervals between injections should be of at least four weeks' duration. The foregoing doses have been observed thus far to be well tolerated and no untoward incidents worthy of mention have been reported. If in exceptional instances a severe, medically authenticated reaction should be manifested, repetition of the inoculation is contraindicated.

Pneumothorax in Pulmonary Tuberculosis

At the Woman's Tuberculosis Center of the General Hospital in Hamburg-Eppendorf, which institution serves as the university clinic, 298 patients underwent treatment with pneumothorax from 1923 to 1933. Dr. C. Mumme, head physician of the center, who recently reported his observations, has noted latterly a greater utilization of active therapy in pulmonary tuberculosis. In a general hospital, as contrasted with a sanatorium, the tuberculous patients will, for the most part, present the disease in an advanced stage unsuitable for collapse therapy. In 302 performances of pneumothorax and 4,358 refilling operations, not one serious complication, such as embolism or fatal hemorrhage, occurred. If an artificial pneumothorax was complicated by a spontaneous pneumothorax (and this is more likely to occur in bilateral than in unilateral pneumothorax) the valvular pneumothorax was already closed if the air was drawn off with the refilling apparatus. Indeed, this was accomplished more quickly if several hundred cubic centimeters of air was removed from the artificial pneumothorax of the opposite side. In fifty-three cases there was a sinus exudate, in fifty cases a moderate exudate and in five cases an exudate so copious that puncture became necessary. During the last three years of the period studied, bilateral pneumothorax was performed in thirty-eight cases and these interventions were much better tolerated than the unilateral. Even in an apparently high grade bilateral collapse (one which, according to the roentgenogram, involved one fourth of the volume of both lungs) no injury appeared for, although the total capacity was markedly diminished, the residual air and the normal capacity underwent only

slight reduction. Favorable results were obtained even in some cases of severe cavernous pulmonary tuberculosis accompanied by laryngeal tuberculosis. Pneumothorax ought therefore to be attempted even in apparently hopeless cases, provided the disease is not yet present outside the organs of respiration.

Studies of Otitis Media and Eustachitis

Dr. Zöllner of the ear clinic at the University of Jena has utilized on a large scale a new diagnostic technic in otitis media and eustachitis. He has found that the permeability of the tuba auditiva can be evaluated by microscopic observation of the membrana tympani. This procedure has elucidated the heretofore vague concepts of "tubal catarrh." The disease conditions loosely classified under this heading run a course marked by similar manifestations, but Zöllner by means of precise observation has been able to subdivide these disorders into separate entities that are of disparate etiology and therefore require varied therapy. A genuine catarrhal inflammation of the tuba auditiva or of the middle ear may always be recognized by alterations in the membrana tympani, such as wrinkling, atony and changes in color. Permeability of the tuba auditiva may be badly impaired or may be normal. Actual constriction or occlusion of the tube is rare. In only a few cases is there a question of permanent cicatricial stenosis or stenosis from tumors. A third and not yet sufficiently well understood group of disorders is probably based on alterations of the middle ear. The tubes are in such cases usually permeable. Massage of the membrana tympani will improve the hearing. Still another group of patients present a pathologic dilatation of the tuba auditiva instead of a constriction. This condition is easily overlooked on superficial examination but may be detected with certainty by microscopic studies of the respiratory movements in the membrana tympani. The therapy demanded by cases of catarrhal inflammations is predominantly directed to the nasopharynx. In severe stenosis complicated surgical measures may be necessary, even a direct bouginage through the nasopharynx. Zöllner was able to remove a complete bilateral occlusion of the nasopharynx by a plastic operation. In abnormal dilatation of the tube, stimulation therapy directed to the mucosa or a plastic constriction is indicated.

Acute Anterior Poliomyelitis in Apes

At Cologne in 1934 two cases of acute anterior poliomyelitis in chimpanzees were reported. Recently another case of a chimpanzee suffering from spontaneous infection with the same disease was reported, also at Cologne. The minister of the interior has ordered that anthropoid apes in the zoological gardens should be closely observed for possible signs of the disease.

BUENOS AIRES

(From Our Regular Correspondent)

Nov. 2, 1937.

New Building for Medical School

The cornerstone for the new building of the Faculty of Medicine of Buenos Aires was laid August 9, during memorable ceremonies. The president of the country, the cardinal archbishop and delegates from Bolivia, Chile, Paraguay and Uruguay were present. The new building will cover an area of 132,500 square meters and will be constructed in a large block. The cost of construction is estimated at 16,000,000 Argentine pesos ($5,000,000). The center of the building will be occupied by a library of 800,000 books, with a reading room for 1,000 persons and smaller reading rooms. The school of medicine will occupy the main front part of the building. It will be an eighteen-story building with headquarters for directors, offices for administration and rooms for teaching histology, physiology, biochemistry, toxicology, hygiene, microbiology and parasitology. The school of odontology will be located near the front part of the building. The classes in the faculty were increased during the last year from six to twenty. The school of pharmacy will be a nine-story building at a lateral front part of the building. It will have teaching rooms and museums. Teaching rooms of topographic and descriptive anatomy and operative medicine will be located in the other lateral front part of the building. The department will have a museum of anatomy 1,850 square meters in size. There will be a large assembly hall with room for 1,000 persons, special teaching rooms for each class, and wardrobes for 4,000 medical students,

New building of Faculty of Medicine of Buenos Aires.

3,000 students of dentistry and 1,000 students of pharmacy. The basement will be commodious, with parking space for automobiles and elevators for each of the different departments. The work of construction will begin before the end of the present year. Dr. José Arce, the dean of the faculty, gave orders to demolish the building which is now the faculty of medicine and which occupied the fourth part of a block. The building will be entirely demolished in November of this year. Near the building a hospital for clinical work will be constructed. It will have 2,000 beds.

Marriages

CHARLES OTTO REINHARDT, Mascoutah, Ill., to Miss Agnes Potasik of Lincoln, in Chicago, September 18.

EDWIN R. TALBOT, Joliet, Ill., to Miss Dorothy Constance Hoyt at Miami Beach, Fla., October 15.

CLYDE MALVERNE STUTZMAN JR. to Miss Emily Albright, both of Williamsport, Pa., September 25.

SAMUEL LOGAN STEPHENSON JR. to Miss Dorothy D. Compton, both of Fairfield, Ala., October 30.

WILLIAM ROBERTS TYSON to Miss Elizabeth Gertrude Ehringhaus, both of Norfolk, Va., October 4.

CHARLES MAXWELL COE, Wakefield, Neb., to Miss Miriam Hobson of Carson, Iowa, October 31.

JOHN B. TOBIAS, Wilkes-Barre, Pa., to Mrs. Katherine Morgan of Scranton, September 15.

JAMES DANIEL ROYSTER, Elm City, N. C., to Miss Virginia Dean, in Halifax, Va., August 16.

EDGAR WALTER STEPHENS JR., Atlanta, Ga., to Miss Ida Lee Mattison of Augusta, October 15.

EDWARD S. MALONEY, Omaha, to Miss Genevieve Mills of Santa Rosa, Calif., October 28.

HUGH WEST, Deland, Fla., to Miss Elizabeth Ann Rhett, in Davidson, N. C., October 9.

PHILIP NAUMOFF, Pittsburgh, to Miss Esther Zuckerman of Durham, N. C., August 21.

MELVIN REESE GUTTMAN to Miss Eleanor Given, both of Chicago, December 5.

Deaths

Blase Cole ✠ Newton, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1907; in 1937 member of the House of Delegates of the American Medical Association; member of the Court of Errors and Appeals; formerly state senator; served during the World War; bank president; on the staff of the Newton Memorial Hospital; aged 57; died, September 30, of injuries received in an automobile accident.

William Preston Holt Jr., Erwin, N. C.; Jefferson Medical College of Philadelphia, 1926; member of the Medical Society of the State of North Carolina and the Southeastern Surgical Congress; past president of the Harnett County Medical Society; aged 36; on the staff of the Good Hope Hospital, where he died, October 7, of an injury received in a fall.

George Crarer McIntyre, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1915; fellow of the American College of Surgeons; served with the Canadian Army during the World War; formerly junior demonstrator in clinical surgery at his alma mater; on the staff of the Toronto General Hospital; aged 52; died, September 27.

Raymond Spear ✠ Medical Director, Captain, U. S. Navy, retired, Coronado, Calif.; Jefferson Medical College of Philadelphia, 1895; fellow of the American College of Surgeons; entered the navy in 1897 and retired in 1930 for incapacity resulting from an incident of the service; aged 64; died, September 28, of chronic myocarditis.

Nehemiah Irving Stebbins, Nashville, Ark.; University Medical College of Kansas City, Mo., 1904; member of the Arkansas Medical Society; formerly professor of operative gynecology at the St. Louis College of Physicians and Surgeons; on the staff of the Nashville Hospital; aged 68; died, September 21.

Ernest Lee Cox, Jacksonville, N. C.; University of Maryland School of Medicine, Baltimore, 1889; member of the Medical Society of the State of North Carolina; past president and secretary of the Onslow County Medical Society; formerly county health officer; aged 72; died, September 17, of chronic myocarditis.

William Neuss, Yaphank, N. Y.; Bellevue Hospital Medical College, New York, 1889; member of the Medical Society of the State of New York; served during the World War; aged 71; on the staff of the Swedish Hospital, Brooklyn, where he died, September 22, of empyema of the gallbladder and bronchopneumonia.

Frederick Otis Morse, Newburyport, Mass.; Tufts College Medical School, Boston, 1897; member of the Massachusetts Medical Society; for many years examiner for the Metropolitan Life Insurance Company; aged 77; died, September 22, in the Anna Jacques Hospital, of cerebral hemorrhage and hypostatic pneumonia.

George Cullen, Galveston, Texas; Northwestern University Medical School, Chicago, 1900; medical director of the American National Insurance Company; formerly medical director of the Illinois Life Insurance Company; aged 62; died, September 4, of angina pectoris, near Bay St. Louis, Miss., en route to Florida.

Gibbs Chisholm ✠ Newark, N. J.; Howard University College of Medicine, Washington, D. C., 1919; served as examining physician in the child hygiene division of the city health department; aged 45; died, September 17, in the Community Hospital, of Addison's disease and pulmonary tuberculosis.

Olafur Bjornson, Winnipeg, Manit., Canada; Manitoba Medical College, Winnipeg, 1897; professor emeritus of obstetrics at his alma mater; fellow of the American College of Surgeons; aged 67; died, October 3, in the Winnipeg General Hospital, of carcinoma of the descending colon.

Harold Boyce Markham, Marquette, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1912; member of the Michigan State Medical Society; formerly connected with the U. S. Public Health Service; aged 52; died, September 22, of pneumonia.

Francis Eugene Salley, Lancaster, S. C.; Medical College of the State of South Carolina, Charleston, 1935; member of the South Carolina Medical Association; aged 29; died, September 23, in a hospital at Charlotte, N. C., of injuries received in an automobile accident.

Joseph J. Anthony Ryan, Chatham, N. J.; Georgetown University School of Medicine, Washington, D. C., 1934; member of the Medical Society of New Jersey; aged 33; died, September 25, in St. Michael's Hospital, Newark, of pulmonary tuberculosis.

George T. Cranford, Seminary, Miss.; Memphis (Tenn.) Hospital Medical College, 1898; member of the Mississippi State Medical Association; formerly county health officer; aged 60; died, September 30, in the Methodist Hospital, Hattiesburg, of pneumonia.

Warren D. Wellman, Jamestown, N. Y.; Eclectic Medical Institute, Cincinnati, 1881; past president of the Chautauqua County Medical Society; on the staff of the Jamestown General Hospital; aged 82; died, September 18, of carcinoma of the rectum.

Louis Josiah Leech ✠ West Branch, Iowa; State University of Iowa College of Medicine, Iowa City, 1881; Civil War veteran; aged 91; died, September 23, in the Methodist Hospital, Madison, Wis., of arteriosclerosis and fracture of the femur.

John S. Zimmermann, Youngstown, Ohio; Western Reserve University Medical Department, Cleveland, 1895; formerly member of the city board of health; aged 73; on the staff of the Youngstown Hospital, where he died, September 23.

William Everett Quin, Fort Payne, Ala.; Kentucky School of Medicine, Louisville, 1881; member of the Medical Association of the State of Alabama; formerly secretary of the De Kalb County Medical Society; aged 86; died, September 17.

Mabel T. Bell, Ventura, Calif.; College of Physicians and Surgeons of San Francisco, 1920; member of the California Medical Association; medical director of the Ventura School for Girls; aged 57; died, September 27, of myocarditis.

Felix Marcus Tully Tankersley ✠ Montgomery, Ala.; Tulane University of Louisiana School of Medicine, New Orleans, 1923; served during the World War; aged 39; died, September 22, following an operation for appendicitis.

Samuel McChesney Ryburn, Morristown, Tenn.; Hospital College of Medicine, Louisville, Ky., 1905; member of the Tennessee State Medical Association; on the staff of the Morristown General Hospital; aged 60; died, September 22.

Oscar Francis Broman ✠ Greeley, Colo.; Grand Rapids (Mich.) Medical College, 1903; served during the World War; past president of the Weld County Medical Society; aged 62; died, September 5, of acute intestinal obstruction.

Edwin Melville Adams ✠ Gridley, Ill.; Barnes Medical College, St. Louis, 1901; aged 60; on the staffs of St. Joseph Hospital and the Mennonite Hospital, Bloomington, where he died, September 26, of cerebral hemorrhage.

William John Malcolm Armstrong, Mitchell, Ont., Canada; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1889; Bellevue Hospital Medical College, New York, 1889; aged 79; died, September 14.

George Thompson, Norwich, Conn.; Medical School of Maine, Portland, 1889; member of the Connecticut State Medical Society; aged 76; died, September 17, of trauma by fall, fractured left hip and bronchopneumonia.

Harvey Hay Bemis, Detroit; Detroit College of Medicine and Surgery, 1921; professor of physical diagnosis, Wayne University College of Medicine; aged 41; died, October 7, of essential hypertension and myocarditis.

Francis Patrick McKenna, Boston; Harvard University Medical School, Boston, 1892; member of the Massachusetts Medical Society; aged 69; died, September 11, of arteriosclerosis and cerebral hemorrhage.

David Barringer Phillips ✠ Youngstown, Ohio; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1910; served during the World War; aged 58; died, September 22, in Phoenix, Ariz.

John Sherwood McBride, Ansley, La.; Louisville (Ky.) Medical College, 1886; past president of the Jackson-Lincoln-Bi-Parish Medical Society; aged 77; died, September 13, in the Methodist Hospital, Alexandria.

Arthur Edward Brides ✠ Stoughton, Mass.; University of North Carolina School of Medicine, Chapel Hill, N. C., 1910; served during the World War; aged 52; was found dead in bed, September 25, of heart disease.

John A. Newcome, Vandergrift, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1892; member of the Medical Society of the State of Pennsylvania; aged 72; was found dead in his office, September 23.

Henry Sisson Cooper, Denver; University of Colorado School of Medicine, Denver, 1914; member of the Colorado State Medical Society; aged 46; died, October 15, in Nucla, of cerebral hemorrhage.

John William Summers, Walla Walla, Wash.; Kentucky School of Medicine, Louisville, 1892; served at various times as a member of Congress; aged 67; died, September 25, of cerebral hemorrhage.

Onofrio La Raja, Scranton, Pa.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1905; aged 56; died, September 24, in the Retreat Home and Hospital, Retreat, of arteriosclerosis.

Duncan U. Saunders, Eloise, Mich.; Detroit College of Medicine, 1906; assistant superintendent of the Eloise Hospital; aged 63; died, September 25, of injuries received when struck by an automobile.

Weston Olin Smith, Alameda, Calif.; University of California Medical Department, San Francisco, 1891; past president of the city board of health; aged 69; died, September 20, in a local sanatorium.

Charles Alsop De Witt Jr., Louisville, Ky.; University of Louisville School of Medicine, 1930; aged 32; died, September 24, in the Vermillion County Hospital, Clinton, Ind., of pneumonia.

George P. A. Gunther, Boston; University of Pennsylvania Department of Medicine, Philadelphia, 1894; aged 84; died, September 5, in Westborough, of coronary sclerosis and chronic nephritis.

James Joline Reed, Pasadena, Calif.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1888; aged 77; died, September 22, of chronic myocarditis.

Robert Putnam Goodkind, Boston; Harvard University Medical School, Boston, 1929; aged 34; died, September 3, in the Massachusetts General Hospital, of subacute bacterial endocarditis.

William Thomas Dempsey, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1905; aged 67; died, October 19, of chronic interstitial nephritis and uremia.

George W. Ragan, Cold Spring, Ky.; University of Louisville Medical Department, 1891; state senator; for many years bank president; aged 72; died, September 27, of heart disease.

Gilman Wayne Stauffer, Akron, Ohio; Ohio Medical University, Columbus, 1901; formerly on the staff of the City Hospital; aged 61; died, September 18, of cerebral hemorrhage.

Albert S. Reiter, Myerstown, Pa.; College of Physicians and Surgeons, Baltimore, 1882; aged 79; died, September 1, in the Good Samaritan Hospital, Lebanon, of arteriosclerosis.

Ulysses S. Grant Arnold, Martinsburg, Mo.; Washington University School of Medicine, St. Louis, 1896; aged 72; died, September 19, in Rochester, Minn., of adenomatous goiter.

Joel Buford Scholl, Jabez, Ky.; Louisville Medical College, 1893; member of the Kentucky State Medical Association; formerly county health officer; aged 70; died, September 4.

Lewis Ryans, Louisville, Ky.; University of Louisville Medical Department, 1904; formerly state senator; aged 66; died, September 26, of arteriosclerosis and endocarditis.

Jesse McCampbell Reed, Magnolia Springs, Ala.; University of Alabama School of Medicine, Mobile, 1914; served during the World War; aged 47; died, September 21.

Alvah Clayton Bridges, Kahoka, Mo.; St. Louis College of Physicians and Surgeons, 1899; also a druggist; aged 67; died, September 5, of cardiovascular degeneration.

Charles Edward Davis, Cassopolis, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1874; aged 93; died, September 28, of influenza.

John W. Sitton ⊕ Alvarado, Texas (licensed in Texas, under the Act of 1907); owner of a hospital bearing his name; aged 70; died, September 20, of angina pectoris.

Herman Isaac Edward Blackmon, Fort Worth, Texas.; Meharry Medical College, Nashville, Tenn., 1932; aged 36; was found dead, October 1, of cerebral hemorrhage.

William Mead Sams, Kansas City, Mo.; Kansas City Medical College, 1896; aged 71; died, in September, at the Kansas City General Hospital, of coronary thrombosis.

Emma Eliza Bower, Ann Arbor, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1883; aged 87; died, October 11, of cerebral hemorrhage.

William Meade Eggleston, Vicksburg, Miss.; Washington University School of Medicine, Baltimore, 1875; aged 81; died, September 19, of malignancy of the pancreas.

Joseph Ewing Cowperthwaite, Butte, Mont.; Chicago Homeopathic Medical College, 1896; aged 64; died, September 15, of coronary occlusion and arteriosclerosis.

John E. Reeves, Orange, Texas; Louisville (Ky.) Medical College, 1894; formerly city and county health officer; aged 69; died, September 20, of cerebral hemorrhage.

Michael Ravn, Merrill, Wis.; Kongelige Frederiks Universitet Medisinske Fakultet, Oslo, Norway, 1880; aged 85; was accidentally drowned, September 30.

Herbert Sawyer McCasland, Moriah, N. Y.; University of Vermont College of Medicine, Burlington, 1904; aged 71; died, September 24, of cerebral hemorrhage.

George Porter Shidler, Torrance, Calif.; Northwestern University Medical School, Chicago, 1907; aged 55; died, September 12, of chronic myocarditis.

Lemuel Fitch Pattengill, Whitesboro, N. Y.; University of the City of New York Medical Department, 1880; aged 85; died, September 13, of mucous colitis.

Harriett Beecher Ward, San Francisco; Hahnemann Medical College and Hospital, Chicago, 1896; aged 76; died, September 30, of coronary occlusion.

Frank L. De Wolf, San Bernardino, Calif.; Kansas City (Mo.) Homeopathic Medical College, 1892; aged 74; died, October 11, of cerebral hemorrhage.

Marie A. Ames, North Platte, Neb.; John A. Creighton Medical College, Omaha, 1901; aged 74; died, September 6, of heart disease and diabetes mellitus.

Benjamin Stilwell Penn ⊕ Humboldt, Tenn.; Vanderbilt University School of Medicine, Nashville, 1892; aged 64; died, September 26, of angina pectoris.

Jay Stephen Malloy, Indianapolis; American Medical College, Indianapolis, 1896; aged 79; died, September 26, of chronic myocarditis and arteriosclerosis.

Michael Joseph Murphy, Providence, R. I.; Bellevue Hospital Medical College, New York, 1893; aged 67; died, September 26, of coronary disease.

Walter Ambrose Huber, Hilliards, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1905; aged 57; died, September 29, of carcinoma.

Louis Fourgeaud, Breaux Bridge, La.; University of Louisiana Medical Department, New Orleans, 1883; aged 81; died, September 10.

Isaac N. Cottle, Oklahoma City; Kentucky School of Medicine, Louisville, 1903; aged 59; died, October 9, of acute dilatation of the heart.

Thomas Albert Weaver, Blachleyville, Ohio; Toledo Medical College, 1898; aged 67; died, September 30, of influenza and edema of the lung.

Charles Edwin Marshall, Buffalo; Albany (N. Y.) Medical College, 1893; aged 66; died, September 28, of chronic nephritis and myocarditis.

Edwin L. Clark, Rockford, Ill.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1883; aged 88; died, October 21, of senility.

Clarence William Taylor, Glendale, Calif.; University of Louisville (Ky.) Medical Department, 1912; aged 52; died, September 11.

Dayton H. Hornor, Roseville, Calif.; Illinois Medical College, Chicago, 1899; aged 69; died, August 18, of coronary occlusion.

Claude B. Rather, Bullard, Texas; University of Louisville (Ky.) Medical Department, 1890; aged 68; died, August 31, of nephritis.

John Scott, Hazleton, Pa.; Baltimore University School of Medicine, 1904; aged 65; died, September 12, of chronic myocarditis.

H. Ellen Walker Berry, Erie, Pa.; Cleveland Medical College, 1893; aged 68; died, October 6, of cerebral hemorrhage.

Frank R. Blackshere, Colorado Springs, Colo.; Barnes Medical College, St. Louis, 1898; aged 70; died, September 20.

John H. Conway, Atlanta, Ga.; University of Georgia Medical Department, Augusta, 1884; aged 81; died, October 7.

Jesse Lewis Rains, Seattle, Wash.; Jefferson Medical College of Philadelphia, 1905; aged 60; died, September 27.

Robert L. Mercer, Shelby, Miss.; Hospital College of Medicine, Louisville, Ky., 1904; aged 69; died, September 10.

R. W. Bryant, Moultrie, Ga.; Atlanta Medical College, 1895; aged 67; died, September 19, of heart disease.

Wade Sperry, Hamburg, Iowa; Ensworth Medical College, St. Joseph, Mo., 1895; aged 76; died, September 1.

Simon P. Berns, Willow Hill, Ill.; Missouri Medical College, St. Louis, 1881; aged 78; died, September 24.

Joseph K. Baker, Mooresburg, Tenn. (licensed in Tennessee in 1913); aged 68; died, September 20.

Bureau of Investigation

MISBRANDED "PATENT MEDICINES"

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the United States Department of Agriculture

[EDITORIAL NOTE: The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the composition; (4) the type of nostrum; (5) the reason for the charge of misbranding, and (6) the date of issuance of the Notice of Judgment—which may be considerably later than the date of the seizure of the product.]

Diaplex.—H. W. Pierce, Denver. Composition: Essentially plant material (not named), largely stems, with a small proportion of saltbush. Fraudulently represented as a safe substitute for insulin in diabetes.—[*N. J. 25838; January 1937.*]

Hem-Roid.—Dr. Leonhardt Co., Buffalo, N. Y. Composition: Essentially extracts of plant drugs including aloe and nux vomica; a small amount of witch hazel was found in one sample. Fraudulently represented as a remedy for "piles."—[*N. J. 25839; January 1937.*]

Adams Vapour Ointment.—Adams Paper & Specialties Co., Waterloo, Iowa. Composition: Essentially menthol, camphor, rosin and petrolatum. For asthma, catarrh, croup, boils, etc. Fraudulent therapeutic claims.—[*N. J. 25840; January 1937.*]

Adams Menthol Salve.—Adams Paper & Specialties Co., Waterloo, Iowa. Composition: Essentially menthol, rosin and petrolatum. For nervous headaches, muscular rheumatism, nasal catarrh, etc. Fraudulent therapeutic claims.—[*N. J. 25840; January 1937.*]

Adams Painon Liniment.—Adams Paper & Specialties Co., Waterloo, Iowa. Composition: Essentially the oils of petroleum, pine-needles and sassafras. Fraudulent therapeutic claims.—[*N. J. 25840; January 1937.*]

Gowans Preparation.—Gowan Chemical Co., Baltimore. Composition: Essentially volatile oils, including wintergreen, camphor, eucalyptol, menthol and turpentine, with carbolic acid, in a fatty base such as lard. For pleurisy, spasmodic croup, pneumonia, etc. Fraudulent therapeutic claims.—[*N. J. 25842; January 1937.*]

B L & K R.—B L & K R Medicine Co., North Chattanooga, Tenn. Composition: Essentially epsom salt, extracts of plant drugs, alcohol (4 per cent), salicylic acid (0.2 per cent), and water, wintergreen flavored. For sore stomach, heart disturbances, etc. Fraudulent therapeutic claims.—[*N. J. 25843; January 1937.*]

Alkavis.—Williams Mfg. Co., Cleveland. Composition: Saltpeter, salicylic acid, an extract of a plant drug, glycerin and water. For rheumatism, kidney, liver and blood disorders. Fraudulent therapeutic claims.—[*N. J. 25844; January 1937.*]

Alcothol-Rub.—Fallis, Inc., New York. Composition: In one lot, essentially alcohol (2 per cent), water, small proportions of glycerin, formaldehyde and perfume; in another lot, essentially isopropyl alcohol (2.1 per cent) and water. Misbranded because of false and misleading representation that the stuff consisted essentially of alcohol, whereas it was largely water; and because of the claim that it was "endorsed by the medical profession," whereas the medical profession, as a whole, had not endorsed the product.—[*N. J. 25845; January 1937.*]

Carboil.—McKesson-Berry-Martin Co., Nashville, Tenn. Composition: Essentially chloral hydrate (9.5 grains per ounce) and tar oil, in an ointment base, largely petrolatum. Fraudulently represented as a remedy for boils, skin disorders, etc.—[*N. J. 25847; January 1937.*]

Novo Iodine Compound.—Union Products Co., New York. False and misleading representations that it was an iodine compound, whereas it was a mixture of chloramine and potassium iodate.—[*N. J. 25848; January 1937.*]

Kopp's Alcohol.—C. Robert Kopp, Inc., York, Pa. Composition: Morphine sulfate (⅛ grain per fluid ounce), flavoring oils including anise oil, with alcohol, sugar and water. Fraudulently represented as a safe and proper medicine for infants and young children.—[*N. J. 25849; January 1937.*]

Slim.—Forest Hill Pharmaceutical Co., East Cleveland, Ohio. Composition: Capsules, each containing 1 grain of dinitrophenol, in milk sugar. Fraudulently represented as a safe treatment for obesity.—[*N. J. 25850; January 1937.*]

Eucaline (Regular).—Eucaline Medicine Co., Dallas, Texas. Composition: Essentially quinidine and cinchonidine alkaloids (4.58 grains per fluid ounce), iron chloride, an extract of a laxative plant drug, eucalyptus oil and a small amount of alcohol, with sugars and water. For malaria, chills, fever, etc. Fraudulent therapeutic claims.—[*N. J. 26119; February 1937.*]

Hawley's Ointment.—Vincent Laboratories, Texarkana, Texas. Composition: Essentially lanolin, camphor and boric acid. Fraudulently represented to prevent influenza and to be a remedy for catarrh, hay fever, croup, etc.—[*N. J. 26120; February 1937.*]

Melatol.—Melatol Laboratories, Oakland, Calif. Composition: Essentially a crude oil. Fraudulently represented as a remedy for diabetes, stomach and kidney disorders, etc.—[*N. J. 26121; February 1937.*]

Dabon Brushless Modern Shaving Cream.—Nostane Products Corp., Brooklyn. Composition: Essentially stearic acid, potassium stearate and unsaponifiable matter, emulsified with a large proportion of water. Fraudulently represented as an antiseptic and a healing agent.—[*N. J. 26124; February 1937.*]

Zann-Ite.—Richard I. Morgan, Toppenish, Wash. Composition: A light brown clay containing 13.5 per cent of water, 51 per cent of silica, and 20 per cent of aluminum and iron oxides, with traces of calcium, magnesium and carbonates. Fraudulently represented to cure diabetes, goiter, rheumatism, heart, kidney and stomach disorders, etc.—[*N. J. 26128; February 1937.*]

Mims' (J. H.) Iron Tonic.—J. H. Mims Medicine Co., Jacksonville, Fla. Composition: A watery solution of iron, with sulfuric, hydrochloric and tartaric acids, colored with a red dye. Fraudulently represented as a remedy for indigestion, dropsy, eczema, rheumatism, pellagra, etc.—[*N. J. 26132; February 1937.*]

Browns (Dr.) Baby Oil.—Nostane Products Corp., Brooklyn. Composition: A neutral mixture of mineral and fatty oils, with a small amount of thymol. Fraudulently represented as an antiseptic and germicide.—[*N. J. 26124; February 1937.*]

Sys-Tone.—Manufacturer not named. Composition: Essentially phosphorus compounds and calcium salts, strychnine, benzoic acid, alcohol, sugar and water. Fraudulently represented as a remedy for tuberculosis, asthma, anemia, blood, glandular and tissue disorders, etc.—[*N. J. 26138; February 1937.*]

Stock's Nu-Tone Tonic.—Manufacturer not named. Composition: Essentially extracts of plant drugs including a laxative, with alcohol, water, salicylic acid, and small amounts of sodium and calcium carbonates. For kidney, liver and stomach disorders, rheumatism, etc. Fraudulent therapeutic claims.—[*N. J. 26138; February 1937.*]

DeWitt's Cough Syrup.—Manufacturer not named. Composition: Essentially ammonium chloride, chloroform, alcohol, sugar and water. Fraudulent therapeutic claims.—[*N. J. 26138; February 1937.*]

DeWitt's Vaporizing Balm.—Manufacturer not named. Composition: Essentially volatile oils including menthol, eucalyptol and camphor, in petrolatum. Fraudulently represented as a remedy for hay fever, nasal catarrh, headache, inflammations, etc.—[*N. J. 26138; February 1937.*]

Red Cross Headache and Neuralgia Remedy.—Manufacturer not named. Composition: Essentially salicylic acid, acetates, common salt and water. Fraudulent therapeutic claims.—[*N. J. 26138; February 1937.*]

Bi-Sarcol.—Bi-Sarcol Laboratories, New York. Composition: Essentially extracts of plant drugs including licorice, with small amounts of inorganic compounds, such as magnesium and calcium, and 96 per cent of water. Fraudulently represented as increasing the red corpuscles, stimulating the digestive juices, toning the kidneys, etc.—[*N. J. 26140; February 1937.*]

Bees Laxative Cough Syrup.—Manufacturer not named. Composition: Essentially ammonium chloride, sugar and water. Fraudulent therapeutic claims.—[*N. J. 26138; February 1937.*]

Nevah Tablets.—Nevah Laboratories, Lock Haven, Pa. Composition: Aminopyrine (1.6 grains), sodium salicylate (2.8 grains), colchicin, magnesium oxide, pumice and starch. For pains of rheumatic fever, gout, neuritis, etc. Fraudulent therapeutic claims.—[*N. J. 26151; February 1937.*]

Diatone.—Diabetic Diatone, Inc., Chicago. Composition: Essentially a starch digestant, such as pancreatin, with salt and clay. Fraudulently represented as a remedy for diabetes.—[*N. J. 26154; February 1937.*]

Kirby's Miracle Mineral.—Kirby's Mineral Products, Union, S. C. Composition: A solution of iron sulfate in water. Fraudulently represented as a remedy for venereal diseases, female disorders, pyorrhea, etc.—[*N. J. 26155; February 1937.*]

APCO No. 36 Antiseptic Suppositories.—Ampere Products Co., West Orange, N. J. Composition: Gelatin capsules containing essentially boric acid, quinine sulfate and cocoa butter. For "feminine hygiene," leukorrhea, etc. Fraudulent therapeutic claims.—[*N. J. 26166; February 1937.*]

Old Indian Herb Laxative.—Pearson Remedy Co., Burlington, N. C. Composition: Essentially extracts of plant drugs including aloe, with alcohol and water. Fraudulently represented as a tonic, blood purifier and a remedy for babies, as well as for eczema, female troubles, gallstones, pellagra, etc.—[*N. J. 26477; May 1937.*]

Videx.—Grove Laboratories, Inc., St. Louis. Composition: Essentially aminopyrine (2.6 grains per tablet) and starch. Fraudulently represented as a remedy for menstrual pains, neuralgia, rheumatism, etc.—[*N. J. 26169, February 1937; and N. J. 26489, May 1937.*]

M. Edouard's B. Acidophilus Compound.—Z. Hubay, Memphis, Tenn. Composition: Essentially a moldy mixture of agar, psyllium seed, milk sugar, starchy material and phenolphthalein (about 2.8 per cent). No significant amount of acidophilus, kelp or dextrin present. Fraudulently represented to contain no purgative, whereas it did contain phenolphthalein; and to change the intestinal flora and "re-mineralize the body and furnish that unbroken chain of vitamins, which is so necessary to perfect health."—[*N. J. 26159; February 1937.*]

Correspondence

"RELATION OF NICOTINIC ACID TO HUMAN PELLAGRA"

To the Editor:—May I call your attention to an error which occurred in THE JOURNAL, October 9, page 1203, in an editorial comment on "Relation of Nicotinic Acid to Human Pellagra." The statement referred to is as follows: "Chittenden and Underhill . . . using diets similar to those associated with human pellagra, were able to produce experimental blacktongue in dogs. They demonstrated that this disease was similar to, if not identical with, human pellagra. Conditions were thus provided for assaying experimentally the various fractions obtained during efforts to concentrate and identify the antipellagra dietary factor."

Reference to the original publications by Chittenden and Underhill and Underhill and Mendel shows that they produced a blacktongue in dogs on a diet containing an abundance of red meat and yeast. Both of these substances will prevent and cure pellagra and the Goldberger type of blacktongue. There have been no assays on pellagra curative material using this Underhill-Mendel type of diet. All the assays in the literature on the pellagra curative factor in blacktongue dogs have been done with the Goldberger type of blacktongue, which was not referred to in your editorial.

In the *Journal of Nutrition,* October 10, in an article entitled "On the Identity of the Goldberger and Underhill types of Canine Blacktongue: Secondary Fusospirochetal Infection in Each," by David T. Smith, Elbert L. Persons and Harold I. Harvey, from the Duke Medical School, it is shown that the clinical picture of blacktongue appears in both types of experimental disease but that the Underhill-Mendel type is probably due to a vitamin A deficiency, while the Goldberger type is the analogue of true pellagra in man.

In view of the great interest which is being aroused in this subject as a result of the discovery of nicotinic acid, I feel that it is important to have the background of this work clearly understood by the whole medical profession.

DAVID T. SMITH, M.D.,
Duke University, Durham, N. C.

NICOTINIC ACID AND VITAMIN B

To the Editor:—In THE JOURNAL, October 9, page 1203, you had an editorial entitled "The Relation of Nicotinic Acid to Human Pellagra." It was with a sense of pleasure that I found that in describing the recent important developments in this field you referred to work of mine, carried out some twenty-five years ago, which dealt with the isolation (and the significance) of nicotinic acid, as obtained from the vitamin B complex.

Rice Polishings

Formula Given	Melting Point	Animal Experiment
I. $C_{20}H_{20}N_4O_6$	233° C.	Not tested
II. $C_6H_5O_2N$ (nicotinic acid)	234° C.	Not tested

You state that "Funk demonstrated that nicotinic acid is a constituent of the naturally occurring vitamin B complex, even though he had apparently assigned the wrong physiologic function to his compound." This statement is incorrect; and I would like, with your kind permission, to present the facts.

The first attempts to isolate vitamin B_1 were made during 1911-1912. The process of fractionation, using yeast and rice polishings, was repeated on a larger scale in 1912, and the results were published in the following year (*J. Physiol.* **46**:173, 1913; *Brit. M. J.* **1**:814 [April 19] 1913). The often repeated statement that my curative crystalline material of 1911-1912 was merely nicotinic acid is based on an erroneous interpretation of my papers. Nicotinic acid was always found to be inactive as a cure for polyneuritis in pigeons. A summary of pertinent data dealing with the experiment carried out in 1913 will be of interest.

I itself was later found to be nothing but nicotinic acid, in perfect agreement with its percentage composition, its melting point and its complete inactivity (when pigeons were used).

Yeast

Formula	Melting Point	Dosage	Activity	Survival
Crude crystalline product	.....	4-8 mg.	Cure in 2-3 hrs.	4-6 days
I. $C_{24}K_{10}O_9N_8$	229° C.	2-8 mg.	Improvement	3-4 days
II. $C_6H_5O_2N$ (nicotinic acid)	235° C.	10-50 mg.	No activity	1-3 days
III. $C_{29}H_{22}O_9N_8$	222° C.	5 mg.	No activity	0-1 day
I and II	.....	{ I, 3-5 mg. } { II, 2 mg. }	Cure in 2-4 hrs.	4-7 days

Even more marked curative results were obtained by combining all three fractions (I, II and III).

It is quite plain, from this summary, that the only claim made for nicotinic acid was that it enhanced the physiologic action when added to the other fraction or fractions—a point of view which is in perfect agreement with our present knowledge of the vitamin B complex. This enhanced action of nicotinic acid and nicotinamide was later confirmed by Szymanska and Funk (*Chem. Zelle u. Gewebe* **13**:44, 1926) and Casimir and Ian C. Funk (*J. Biol. Chem.* **110**:xxxv [April] 1937).

I wish to emphasize, finally, that at no time was nicotinic acid mistaken for vitamin B_1.

CASIMIR FUNK, Rueil-Malmaison, France.

THE RECURRENT LARYNGEAL NERVE

To the Editor:—Granted, I erred, even according to the nomenclature which was my authority, in stating there is only one recurrent nerve. There are two. And Dr. Oscar V. Batson's cross tabulation (THE JOURNAL, November 6, p. 1562) confirms my contention that "the BNA does (not) recognize the recurrent laryngeal nerve." The nerve under consideration is so designated in the British nomenclature. I might add here that Dr. Batson's tabulation also demonstrates to me the futility of quibbling about names in view of the confusion resulting from differing terminologies. However, the BNA, being the consensus of an international congress, may be expected to be more authoritative than the classification of any national group.

A recurrent nerve is one that retraces its course in arriving at its insertion. Neither the maxillary nor the mandibular nor the "many other recurrent meningeal nerves" are recurrent in its anatomic connotation, Dr. Wharton Young to the contrary. An anatomic nomenclature serves the purpose of incisive description. From that standpoint, "recurrent laryngeal," as there is only one (paired) recurrent nerve, is redundant and therefore ambiguous.

There is an anatomic basis for the relative infrequency of right laryngeal paralysis following thyroidectomy and that basis is explicable only in terms of embryologic development. The right inferior laryngeal or recurrent nerve (BNA) or the right recurrent laryngeal nerve (BR), in deference to Drs. Young and Batson, lies to the right of the esophagus whereas the left lies in front of it, in anteroposterior relation, a difference of from 0.5 to 1 cm. in favor of the right for greater depth.

Though the editorial in question (Total Thyroidectomy for Congestive Heart Failure, THE JOURNAL, July 17, p. 210) concerned thyroidectomy primarily and laryngeal paralysis only incidentally, my communication (THE JOURNAL, September 4, p. 809) was concerned chiefly with an anatomic explanation of

the clinical observation of the greater frequency of left laryngeal paralysis following thyroidectomy. From that standpoint it was only relatively in error and the inclusion of mediastinal disease in connection with the subject of laryngeal paralysis was more germane to it than reference to the trigeminal nerve was to the subject of recurrence—and with greater accuracy.

It follows that the editorial did not contain "by implication a gross falsehood"—the error is mine. Nonetheless, in stating that the paralysis "in no instance was bilateral," it was shown that the anatomic basis for the clinical phenomenon was not realized. Had the paralysis been bilateral or only right sided, it would have been the more startling and, of itself, been evidence of shoddy surgery. JOHN F. QUINLAN, M.D., San Francisco.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

DIFFERENTIATION OF HIP, SACRO-ILIAC AND LUMBAR LESIONS

To the Editor:—Please differentiate disorders of the (1) hip joint, (2) lower part of the back and (3) sacro-iliac joint, and the anatomic reasons for the tests. SAMUEL L. IMMERMAN, M.D., Philadelphia.

ANSWER.—In the differentiation of hip, sacro-iliac and lumbosacral disorders the following tests are useful but not always conclusive:

1. Point of tenderness. In hip joint disease, tenderness is commonly found anteriorly over the hip joint capsule. Sacro-iliac involvement may be associated with tenderness over the inferior sacro-iliac ligaments. In lumbosacral disorders, tenderness over the interspinous and the iliolumbar ligaments may be found.

2. Mobility tests. Restricted or painful motion of the hip joint may indicate disease of this joint. Care must be taken to differentiate muscle spasm and restriction due to irritation of the sciatic nerve. Mobility of the lumbar spine is tested with the patient in the standing and sitting positions. In lumbosacral disorders the spine is held rigid in both positions, while in sacro-iliac disorders there may be ability to flex the spine until tightened hamstrings put stress on the sacro-iliac joint. The sitting position facilitates flexion of the spine in sacro-iliac disorders.

3. Manipulative tests. These are done with the patient in recumbency: (*a*) Passive flexion of the two hips at the same time places the lumbosacral joint under stress. (*b*) The straight leg-raising test places stress on the sacro-iliac joint by the pull of the hamstring muscles on the ischium and may reproduce pain in this joint. It also puts tension on the sciatic nerve, and a positive test may be obtained in any condition associated with irritation of that nerve or its roots. (*c*) The Patrick sign, obtained by flexion abduction and external rotation of the thigh, stretches the anterior portion of the hip joint capsule and through it may place stress on the sacro-iliac joint. It may be positive in either hip or sacro-iliac joint disorders. (*d*) The Gaenslen test of hyperextension of one thigh with flexion of the opposite thigh places rotary strain on the sacro-iliac joint. (*e*) Compression of the iliac crests may occasionally reproduce sacro-iliac but not lumbosacral pain.

Thorough roentgenographic study is always indicated and may assist in localizing the disorder.

STAMMERING

To the Editor:—Can you advise me as to the desirability of sedative treatment in cases of stammering in young children, and the way in which it should be employed? WILLIS H. MCGRAW, M.D., Cortland, N. Y.

ANSWER.—Sedative treatment in stammering must, of course, be purely palliative. It has ceased to be invoked in mental hygiene clinics where speech defect cases are thoroughly studied, for two reasons. One is that the dosage of a sedative in a young child, no matter how small, produces untoward symptoms; and even if the drug is practically non-habit forming, such as phenobarbital or bromides, the tendency is for the child to become accustomed to it. A much more serious objection is the fact that it has not produced the results that had been hoped for. Instead, the child should be thoroughly studied as to the emotional, intellectual and physical components that might be behind such stammering, and treatment should be on the basis of psychologic function rather than on sedation. The majority of stammering cases are due to some emotional maladjustment between the child and the parents. This would have to be looked into with a mental hygiene questionnaire, and the treatment based on the cause rather than the symptoms.

CERVICITIS AND PROSTATITIS AS CAUSE OF LEG PAINS

To the Editor:—A woman who had her cervix cauterized, under a local anesthetic, noticed immediately on leaving the table that a partial numbness existed in the left leg, running down into the great toe. This became progressively worse and painful for three days and subsided as healing took place in the cervix. There was no question of pressure, as the legs were not held in straps or supports. The numbness is present in varying degree even after eighteen months and is somewhat better after menstruation. The neurotic element can be excluded. A man with a badly infected prostate complained of feeling the massage all the way to his great toes. He had noticed for months that when his prostate was sore there was pain in the toes, even to the point of making walking difficult; this symptom was relieved when the prostate was less sore and discharge was minimal. The presence of this symptom on massage of the prostate was confirmed by two genito-urinary surgeons who had noticed the same thing. Is this reflex rare? A neurologist consulted by the first patient said he had never heard of it. Is there any suggestion for the relief of numbness and attendant cramps which she complains of, if it is due to the cauterization? The pelvis is otherwise entirely normal.

M.D., Pennsylvania.

ANSWER.—It is difficult to conceive how cauterization of the cervix could be the cause of subsequent numbness in the leg. There is no physiologic or anatomic relationship existing in these areas. Inquiry among several gynecologists of experience fails to elicit a similar observation. It is possible that the patient was placed in such a position that pressure on one of the nerves in the leg was the cause of the pain. It is also possible that the cervix, which is frequently a focus of infection, may have been the cause of a coincidental localized neuritis.

There is also no anatomic relationship between the nerves of the prostate gland and the leg. While pain is frequently observed on vigorous massage of the prostate gland, it is extremely rare to find that the pain extends as far as the toes. The sensitive patient may complain of pain in the lower part of the abdomen, and in some cases the pain may radiate to the hips. The pain in the toes complained of by the patients referred to might be caused by a coincidental neuritis or arthritis subsequent to infection in the prostate gland. In all cases of this kind it would be well to exclude any other possible foci of infection in either teeth or tonsils. It might be advisable to try applications of heat and contrast baths for the numbness and cramps in the leg.

TREATMENT OF CHRONIC PROSTATITIS

To the Editor:—A white man, aged 44, married for the first time five months ago, complains of aching pain in the left knee joint similar to that which he had when he first contracted gonorrhea. At that time (about twenty years ago) he was treated with vaccines and recovered with no disability. He had no epididymitis but had a stricture, which was never treated. At present there is no discharge or "morning drop." Massage of the prostate brings forth a cloudy, whitish fluid. The prostate itself appears soft, symmetrical and not tender. A soft rubber catheter meets resistance in the anterior part of the urethra and obstruction at the membranous portion. The knee joint is not tender, red or swollen, nor is there limitation of motion. The patient works in a slaughter house and frequently passes into and out of the icebox; at times he even remains in it for an hour or so. Glass tests have changed the urine from cloudy to clear, with a lessening in the number of shreds. Smears taken directly from the penis show gram-negative diplococci, intracellular and extracellular, with epithelial and pus cells. The smear taken after prostatic massage shows a similar picture. I have been using potassium permanganate solution for irrigation and 1: 2,000 Silvogon solution for instillations. I hesitate to "sound" the urethra for the stricture for fear of pushing the infection farther up. Can you suggest a procedure for getting a more rapid result? Would intercourse be safe at this stage?

M.D., New York.

ANSWER.—The first question to be decided is whether this patient has gonorrhea. Repeated examinations by Gram's stain and culture of any urethral discharge and of the prostatic secretion should be made to determine the presence of the gonococcus. If this organism is present, of course sexual intercourse must not be allowed. If it is not present, the condition must be treated as chronic nonspecific urethritis and prostatitis with probable stricture. The urethra should be sounded, and if stricture is found it should be dilated even though an exacerbation of symptoms is possible. A thorough search for other

foci in the teeth or tonsils should be made, and if any infection is found it should be eradicated. Then a regular course of prostatic massage, with irrigations of the urethra and bladder if necessary, should be started. One should be careful not to overtreat. It is best to carry on a regular period of treatment for from ten to twelve weeks and to follow this with a rest from all treatment for a similar period. A second course of therapy may be needed. Conditions of this sort are frequently stubborn and prolonged. However, with cooperation and perseverance on the part of the physician and the patient, an eventual cure should be obtained.

FAINTING

To the Editor:—A woman, aged 24, has had trouble with fainting spells ever since she was small. They followed excitement or undue strain. She would come home from a shopping trip and while trying on some of her new clothes would fall in a faint. There is no hysteria; she does not need an audience; neither is there any cry or foaming at the mouth or any convulsions. The patient had fairly regular periods but was given theelin before she could become pregnant. A baby was delivered spontaneously after only six hours of labor. There was considerable postpartum hemorrhage, which was finally controlled. Six days later she began having chills and fever, which was the beginning of a thrombophlebitis in the left iliac veins. She is still in bed. Her progress has been hampered considerably by these fainting spells, which are more severe than any one has seen before. She cannot feel her lower extremities; her head feels like a vacuum. She does not lose consciousness completely. Her blood pressure and pulse remain good; neither is there any change in her temperature. Her red blood count, even after considerable blood loss, is four million and her hemoglobin seventy per cent. The white count was 20,000 but is only 10,000 now. The blood pressure is always low, systolic 105, diastolic 65. The patient is well developed and well nourished and, in my opinion, is going to recover from her present trouble. I should like to know the basis for these "spells." What can be done for her? Is there a glandular dyscrasia? She seems to be normal in every other respect. The thyroid is normal at present, but it did enlarge somewhat with pregnancy. Adipose tissue is distributed normally. The baby was perfect and has remained so, and is bottle fed. M.D., Nebraska.

ANSWER.—Before a definite diagnosis is made in this case, a more complete series of examinations will have to be carried out. This should include a thorough investigation for the possible presence of a brain tumor and for disturbances in the eyes and ears. Hence it is important for a neurologist and otologist to study the patient. Likewise a basal metabolism study should be made and a roentgenogram of the skull taken. If all physical and laboratory examinations fail to reveal a definite cause, it must be assumed that the cause of the fainting spells is a psychic one. If this is the case, a cure can be effected in most instances by a competent psychiatrist or psychoanalyst.

ASTIGMATISM

To the Editor:—A woman, aged 53, complained of tiredness of the eyes and strain after reading. She occasionally saw a blue halo along the edges of printed words. Her glasses were wavy, contained some fine striae, or bubbles, and had a poor grade tint incorporated in the lenses. The ocular tension and the pupillary reactions were normal. Examination of the fundi disclosed no abnormalities. The blood pressure was 135 systolic and 80 diastolic. Corrected vision gave 20/20 in each eye. A first grade colorless lens with an appropriate add for reading was prescribed. The patient returned with the new lenses and is able to see better than formerly, but she still complains that she is disturbed by seeing blue above words and a yellow streak below. Also, is conscious of seeing these colors when outdoors in bright sunlight. She does not have disturbed vision in reduced illumination, and there are no evidences of night blindness. What may be some of the causes for this condition? What can one do for relief? M.D., Indiana.

ANSWER.—The only condition in which a "streak" or "line" is seen above or below or both above and below a given word or line of either the Snellen chart at 20 feet (7.6 meters) or a chart used to test the near vision is uncorrected astigmatism; and patients have never spoken of any color in connection with such doubling of the line. If the blue image is an entirely separate image, astigmatism can be ruled out. If it merges with the image of the word, it probably is an odd astigmatic phenomenon. Blue vision and the like are encountered only after the lens has been removed.

SEMPLE AND PASTEUR RABIES VACCINES

To the Editor:—1. What is the Semple type of antirabies vaccine? 2. How does it differ from a Pasteur antirabies vaccine?

M.D., New York.

ANSWER.—Both vaccines consist of central nervous tissue of rabbits inoculated with the virus of rabies. Pasteur's vaccine consists of emulsions of the spinal cord of such a rabbit, the virus in which has been killed or attenuated by drying the cord. The treatment begins with injections of killed virus and leads gradually up to injections of living virus. Semple's vaccine is nervous tissue of rabbits infected with rabies, the virus in the tissue having been killed completely by mixture with phenol. In this case the treatment consists entirely of the injection of killed virus.

PALLIATIVE TREATMENT OF CANCER

To the Editor:—Is there anything that might be of value in palliative treatment for a patient dying with cancer of the breast aside from narcotics or the usual drugs? She has had a tremendous amount of x-ray treatment since her breast was removed one and a half years ago.

M.D., California.

ANSWER.—Unfortunately, there is no palliative treatment for advanced carcinoma which has any curative value, but much can be done for such patients by judicious manipulation of drugs. For example, the administration of small doses of codeine plus aminopyrine or acetphenetidin and acetylsalicylic acid mixed together may supplant the stronger narcotics, such as morphine or dilaudid, for a time. Each of these opium preparations seems to have a rather different effect on different patients, so that the drugs can be changed after two or three weeks to avoid habituation to one form. In fact, one type of drug may prove far better than any other for a given individual. It is entirely a matter of trial.

Care should be taken to remove fluid from the chest in case it accumulates, as is probable, and small doses of x-rays often relieve bone pains and make the patient feel she is being cared for. These x-ray doses should be given not more than twice a week and should be small in amount. Care should be taken not to use the x-rays over areas in which the skin is damaged by previous irradiation, otherwise extensive ulcerations which are painful may appear. The psychic effect of interest and evident sympathy are valuable even in patients suffering from an incurable disease.

TRAUMA AND CORONARY OCCLUSION

To the Editor:—A man, aged 65, with a past history of active life in regular working hours, tells this story: About 3 p. m. he slipped as he sat leaning in a chair and was thrown into a sharply jack-knifed position between his chair and the wall. He had some discomfort across the lower part of his chest and complained of it several times that night. The following morning at 9 o'clock he experienced a much more squeezing type of pain under the sternum and down the left arm. He became pale and began to sweat profusely. His blood pressure dropped from 134 to 104 during the following forty-eight hours. He had a slight fever of 101.2 F., a leukocyte count of 12,000, a sedimentation time which increased in rapidity by the third day, and an electrocardiogram typical of coronary occlusion. The course was uneventful, the fever disappeared within a week and the sedimentation time reached normal limits within three weeks. There was no past history suggesting coronary sclerosis. His blood pressure has been in the neighborhood of 132 systolic, 80 diastolic. A competent eye man reports that there have never been any arterial changes in the retina. An examination of his peripheral arteries does not at this time reveal any evidence of sclerosis. I would appreciate an opinion as to whether trauma in this case or any other cases might be considered as an etiologic agent in the production of the thrombosis. M.D., California.

ANSWER.—From point of time it does seem as if the coronary thrombosis that developed in this patient was definitely related to the injury. Such relationship cannot ordinarily be established. Coronary thrombosis usually comes out of a clear sky, but there are instances in which injury and strain possibly have helped to precipitate coronary thrombosis in a vessel already badly damaged, perhaps through rupture or dissection of the wall or of a "cholesterol abscess" or of a sclerotic plaque. There are not, however, enough data as yet to make any clear statements about such a relationship.

RENAL CALCULUS AND NEPHRITIS

To the Editor:—In one of two patients with renal calculi lying in the pelvis of the kidney there was renal colic, and in the other no colic but heavy albuminuria without (macroscopic) pyuria. In the latter the calculus was removed by operation and the albuminuria soon ceased. In the former there was macroscopic pyuria but an amount of albumin out of all proportion to the amount of pus. Neither showed any signs of diffuse nephritis such as edema, hypertension, vascular changes or nitrogen retention. What is the pathologic physiology of the albuminuria in these cases? I have difficulty in seeing how glomerular functions can be influenced by a calculus in the kidney pelvis, accepting the fact that protein in such large quantities must escape by way of the glomerular epithelium. M.D., England.

ANSWER.—Albumin is frequently found in large quantities in the urine as a result of renal stone. This may be caused by red blood cells, pus cells or a mucopurulent exudate resulting from secondary irritation in the surrounding renal tissues. These elements usually disappear from the urine following removal of the stone, although they may be present in diminishing degree for a period of several months to a year. It is hardly to be expected that there would be any clinical evidence of

diffuse nephritis, renal insufficiency or vascular changes in the presence of a presumably normal kidney on the other side. In fact, even though renal calculus is present in a solitary kidney, it is seldom that evidence of diffuse nephritis or renal insufficiency results unless there is very extensive destruction of renal tissue. Glomerular functions are undoubtedly influenced by calculus in the kidney, as shown by reflex inhibition of excretion of dye. This may be graphically visualized in the excretory urogram, where a renal calculus often will cause failure of visualization following intravenous injection of solutions of iodine used for urographic purposes. Tests of renal function made by means of dyes such as indigo carmine, when calculus is present, reveal a lessened intensity or the dye return or complete absence. Within a few days after removal of the calculus the function of the kidney will usually be restored to normal, as shown by normal visualization in the excretory urogram. Since it has been shown that the excretion of urographic mediums is largely a glomerular function, it is evident that the glomeruli are directly involved in reflex inhibition of excretion.

PROGRESSIVE MUSCULAR ATROPHY OR LEAD POISONING

To the Editor:—A man, aged 58, for the past fifteen years has been employed in a jewelers' supply shop. During this time his sole job has been to file solder from the joints of rough gold-brass plates. He states he has noticed progressive loss of strength in the hands and arms for a year. Several years ago he had frequent severe headaches, and before that he had attacks of colic in the left lower quadrant of the abdomen, which a physician told him were due to gallbladder trouble. Examination now reveals marked atrophy of the thenar and hypothenar muscles and the interossei, and some wasting of the larger groups of both arms and forearms. The fingers of both hands are contracted into the flexed position seen in Dupuytren's contracture. There is a bilateral double wrist drop. There is constant coarse fibrillary twitching in the muscles of the arms and shoulder girdle. There is some weakness of the lower extremities, and the gait is of the waddling type, but there is no toe drop. There are no sensory changes either subjective or objective. The pupils are equal and regular and they react to light; the fundi are normal except for some tortuosity of the arteries. There is a double false denture. The chest is emphysematous, the lungs hyperresonant; the heart is essentially normal. The blood pressure is 180 systolic, 100 diastolic. The hemoglobin is 70 per cent (Tallqvist). No lumbar puncture has been done. I feel very strongly that this is a case of chronic lead intoxication. There is no lead line, owing to the false teeth. A smear of the blood showed no basophilic stippling with Wright's stain. Would x-ray examination of the long bones demonstrate the presence of lead? What is the procedure for having an analysis of the urine done; i. e., how large a specimen? Assuming that he does have lead poisoning, should treatment be directed toward "delead-ing" him with iodides and acid ash diet, or should he be given calcium and vitamin D?

M.D., Massachusetts.

ANSWER.—This patient's condition sounds more like progressive muscular atrophy than lead poisoning, though occasionally lead poisoning may mimic the latter disease. The diagnosis of lead poisoning necessitates some other objective sign. A roentgenogram of the long bones does not demonstrate the presence of lead in an adult; it is of value in children only before the epiphyses unite. To have an adequate analysis of urine for lead, one should have at least a twenty-four hour specimen. If one assumes that this man does have lead poisoning, it would be wiser to delead him with a low calcium diet, which contains no milk, eggs or green vegetables. To this should be added ammonium chloride in a 20 per cent solution, one teaspoonful six or eight times a day in full glasses of water. This should be continued for about six weeks, after which he should return to a high calcium diet. Iodides may be used but they do not seem to be as effective as the treatment outlined.

FIBROSIS OF PENIS FOLLOWING GONORRHEA

To the Editor:—A white man, aged 66, with a history of gonorrhea forty years ago, has had curvature of the penis on erection for the past six months. The curvature is opposite in direction to that of the usual chordee of gonorrhea. Erection is painless. During an erection the patient is unable to straighten the penis manually. Intercourse is impossible. Ejaculations are present. Physical examination is negative. There is no stricture of the urethra. The prostate is normal. The blood pressure is 170 systolic, 90 diastolic. The urine is normal. There is nocturia from three to eight times resulting from copious drinking of water. Is it possible that there has been a fascial tear or stretching of the fascia on the urethral side, and would it be possible to plicate the fascia on the urethral side or cut fascia on the opposite side so as to allow the penis to be straight on erection? Are there any references?

M.D., New York.

ANSWER.—The condition described is probably caused by a noninflammatory fibrosis involving the corpora cavernosa. It is commonly referred to in the literature as plastic induration of the penis, chronic cavernositis, circumscribed fibrosis, and La Peyronie's disease. La Peyronie gave the first full description of the lesion in 1743.

There is still a difference of opinion as to the nature of the lesion, but apparently it is due to a noninflammatory fibrosis affecting chiefly the smaller vascular sheaths in the corpora cavernosa. Multiple areas of induration are usually found in the penis, most often in the dorsal portion near the base. In some cases there are linear areas of induration which are difficult to palpate. Pathologic examination of the indurated area usually reveals elastic fibrous tissue. Deformity of the penis while in erection, similar to that described, is frequently present and is often painful. The progress of the disease is slow and after reaching a certain stage it usually remains stationary. In many cases the severity of the symptoms will gradually subside.

There is no known effective treatment for this condition. Surgical removal and plastic operations have been tried frequently and have proved unsatisfactory. Better results have been obtained from the use of radium than any other form of treatment. In some instances the plaques are considerably softened and, although they do not usually disappear, they have been so reported in a few cases. In some cases radium has been of distinct benefit in causing amelioration of pain, although the deformity is not usually affected. Patients are often made more comfortable if assured that the disease is not dangerous to life.

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DEXTROSE IN SHOCK TREATMENT OF DEMENTIA PRAECOX

To the Editor:—In reading the literature on insulin shock treatment for dementia praecox, I find reference to a special tube feeding technic that has been devised by Dr. Sakel. Will you kindly describe this technic.

M.D., Indiana.

ANSWER.—The hypoglycemic coma or shock is terminated by Sakel with a tube feeding of from 100 to 150 Gm. of sugar in solution. Water, tea, milk or orange juice may be used. When it is intended to produce a prolonged shock, the tube is inserted prophylactically at the beginning of coma, and its position is checked from time to time by aspiration of gastric juice and a litmus test of its acidity. Dipping the filled funnel below the level of the lung at the beginning of tube feeding will also show, by the absence of bubbles, or by holding it to the ear, that the tube is not in the trachea. Even in severe shock the sugar is quickly absorbed in the stomach. The patient begins to awaken from seven to fifteen minutes after the feeding and is usually completely awake in from half to three quarters of an hour. If vomiting occurs during a tube feeding, the patient is turned on his side and the intravenous administration of sugar is resorted to.

PSYCHOSIS AND HYPERTHYROIDISM

To the Editor:—A woman, aged 46, with a previous history of nervousness and neurasthenia, had a thyroid crisis three years ago, and a mild but definite psychosis developed. The psychosis is expressed by a negativistic and unresponsive attitude coupled with the maintaining of a fixed position in bed, with the arms rigid and flexed. She hears, understands and remembers as well as any one and is slightly responsive to the questions of her husband, who feeds her and attends to her needs. She has a flushed face, a warm and moist skin, eyelids that are closed and tremulous and a hard, fixed adenoma of the right lobe of the thyroid. The lungs are clear, the heart rate varies between 110 and 130 and the weight curve is relatively constant. No metabolic tests, chemical tests of the blood (especially of the calcium and phosphorus) or tests of the renal functions have been performed. Can subjective and objective improvement be expected with a thyroidectomy, especially in the mental status? In general, what is the mental response to a thyroidectomy in persons who have a psychosis as a result of a hyperthyroidism?

M.D.

ANSWER.—A psychosis appearing in a patient with thyrotoxicosis may disappear with the cure of the thyrotoxicosis. The result depends on a good many factors. If the mental symptoms are entirely the result of the thyrotoxicosis, recovery may be expected, but if the toxic state is only an exciting agent for an underlying psychosis, appropriate treatment will leave the patient unchanged as far as the mental symptoms are concerned. There is no definite way to differentiate between these two types of psychotic reaction, for there is nothing characteristic about the mental state which is associated with, or caused

by, thyrotoxicosis. Treatment, however, is usually indicated and certainly should be advocated in this case. If thyrotoxicosis is present, the patient may respond to iodine and this alone may be enough to improve the mental state. If operation is indicated by the presence of adenoma, surgical treatment should be instituted in the hope that it will affect the psychosis. The value of treatment of thyrotoxicosis in cases of mental disease is discussed on pages 433-436 of "The Thyroid and Its Diseases," by Dr. J. H. Means, Philadelphia, J. B. Lippincott Company, 1937.

THYROID ADENOMA

To the Editor:—A woman, aged 24, has an enlargement of the right lobe of the thyroid. This enlargement is the size of an egg and is smooth, uniform and firm but not hard. At times it is more prominent, especially during menstruation. There is occasional difficulty in swallowing. She is in good health with the exception of the following symptoms, which I have associated with the thyroid: constant fatigue, occasional attacks of tachycardia, occasional periods of being very warm, and perspiring hands. There is no perceptible tremor. This swelling was first noticed about a year ago, and the patient states that it has become slightly larger. She has gained 7 pounds (3.2 Kg.) in the past two months. Her present weight is 107 pounds (48.5 Kg.) and she is 64 inches (163 cm.) tall. A basal metabolic test taken March 20 showed a rate of plus 2.4 per cent. Can this type of thyroid, which I have considered a simple goiter, be treated with compound solution of iodine, and if so what would be the proper dosage? Would it be just as well to use iodostarine, giving one tablet daily for thirty days during alternate days? If the latter is recommended, over how long a period should this treatment be carried out? What about surgery?

M.D., Illinois.

ANSWER.—This patient, in all probability, has an adenoma in the right lobe of the thyroid; its change in size with menstruation strengthens this belief. Pressure on the esophagus may account for the occasional occurrence of dysphagia. It is most unusual for an adenomatous goiter to cause hyperthyroidism before the age of 30; therefore the normal basal metabolic rate in this case is to be expected. However, adenomas may cause symptoms such as she has with the basal metabolic rate in normal limits. A neurosis of some type may account for the symptoms.

Malignant degeneration may occur in such an adenoma, even at her age, and the rather rapid development of the enlargement in this instance would make one suspicious of a malignant condition although the chances are against it.

Compound solution of iodine will not cause the tumor to disappear and its use is not indicated, as it has no place in the treatment of goiter except in hyperthyroidism and then only as a preparation for operation.

Iodostarine or any other iodine prophylactic may be used as a prophylactic against the occurrence of goiter during adolescence and pregnancy and as a treatment for colloid goiter with hope of success up to about the age of 24. It will not cause an adenoma of this size to disappear.

Surgical removal of the adenoma is advisable because it may be the site of malignant degeneration and will prevent the occurrence later of hyperthyroidism and cardiac damage. No other treatment will do other than temporarily influence the symptoms. Surgical treatment will in all probability cause the symptoms to disappear, in addition to being good preventive medicine.

PARATHYROID EXTRACT IN HYPERTROPHIC ARTHRITIS

To the Editor:—A patient of mine with long standing chronic hypertrophic arthritis asked me recently about the use of parathyroid extract in her disease. Can you give me some information as to its effectiveness, dangers and contraindications, together with the recommended dosage? I would appreciate it if you would give me some references that I might read.

M.D., Ohio.

ANSWER.—The use of parathyroid extracts in chronic arthritis has been discussed in some detail in Queries and Minor Notes (THE JOURNAL, Oct. 13, 1934, p. 1171) and critical comments on parathyroidectomy for arthritis are included in the recent "Third Rheumatism Review" (*Ann. Int. Med.* **10**:754 [Dec.] 1936). In order to justify the use of parathyroid extracts for arthritis one should be able to demonstrate a consistent abnormality in mineral, especially in calcium, metabolism in this disease, but no such alterations have been found to exist. Recent and previous investigations have failed to show any significant abnormality in the calcium content of the blood or urine of patients either with chronic infectious (atrophic) or with hypertrophic (osteo-) arthritis. In 97 per cent of 100 cases of atrophic and hypertrophic arthritis, Hartung and Greene found normal blood calcium values (*J. Lab. & Clin. Med.* **20**:929 [June] 1935). These results are in agreement with those of Buckley and Race (First Research Report of the Devonshire Hospital, Buxton, Bristol, John Wright & Sons, Ltd., 1928), of Bauer, Bennett and Short (*New England J. Med.* **208**:1935 [May 18] 1933) and of Race (Reports on Chronic Rheumatic Diseases, No. 1, edited by C. W. Buckley, New York, Macmillan Company, 1936).

The abnormalities in bone calcium seen in arthritis (bone atrophy in certain stages of atrophic or rheumatoid arthritis, and marginal bone hypertrophy in hypertrophic or osteoarthritis) are believed to be due not to any general fault in calcium metabolism but to local changes in circulation. It has been shown (Jones, R. W., and Roberts, R. E.: *Brit. J. Radiol.* **7**:321 [June], 391 [July] 1934) that an increased blood supply to bone will produce atrophy, a decreased blood supply to bone will provoke hypercalcification. It is suggested that the atrophy of bone in atrophic arthritis may therefore be due to the increased (no' decreased) capillary circulation which inflamed synovial membrane exhibits and that arteriosclerotic or inflammatory changes in nutrient vessels of joints may be responsible for some of the bone changes seen in hypertrophic arthritis. Part of the latter at least are probably due to inflammation in the periosteum. Parathyroid extracts have been used for arthritis empirically by a few investigators but without much success (for references see previously mentioned note). More recently some have tried to prove that the arthritic patient (with atrophic arthritis or with "ankylosing polyarthritis or spondylitis") needs not more parathyroid extract but less. It is argued that chronic arthritis is a symptom of hyperparathyroidism and that parathyroidectomy is therefore indicated. Some writers have reported that their arthritic patients have derived considerable relief from this. However, histologic examination of the tissues removed at "parathyroidectomy" by one proponent of this idea indicated that from 28 per cent of his improved patients no parathyroid tissue had actually been removed.

Those who have had the largest experience with cases of undoubted hyperparathyroidism in this country refuse to sanction parathyroidectomy for arthritis or to admit that roentgenograms of patients with arthritis or with hyperparathyroidism show common pathologic alterations. It must therefore be concluded that at present there is no rationale for prescribing parathyroid extract or for removing the parathyroids from patients with either atrophic or hypertrophic arthritis.

CYSTOCELE AND BACKACHE

To the Editor:—Is uterine anteflexion of moderate degree, together with a small cystocele of which the patient is unaware, a plausible explanation for disabling backache? The degree of flexion is not sufficient to cause any dysmenorrhea.

M.D., Michigan.

ANSWER.—Anteflexion is not a cause of backache. A cystocele would produce backache only in conjunction with prolapse of the uterus and relaxation of the uterine supports. Of course if there is infection of the urinary tract due to poor emptying of the bladder because of the cystocele, it is possible that the backache might be caused by the focus of infection in the urinary tract.

EXERCISE AFTER NEPHRECTOMY

To the Editor:—Following a nephrectomy in which there was the usual incision with the division of muscles but no infection and primary repair, what in your opinion is the length of time required before a woman might return to active sports, such as golf?

M.D., Illinois.

ANSWER.—In the average noninfected case with good repair of the wound following nephrectomy, strenuous exercise such as golf should usually be withheld for a period of at least two months after healing. There are some factors, however, which may extend this interval. In case of a thick muscular or fatty abdominal wall it may be advisable to wait until a period of three months has elapsed. Subsequent muscular weakness in the wound is apt to result from accidental severing of the nerve supplying the area involved rather than from violent postoperative exercise.

AMENORRHEA WITH INFANTILISM

To the Editor:—A 15 year old girl whose menses have not yet started developed an acute condition of the abdomen. A strangulated right ovarian cyst was removed. It measured about 2 by 3 inches; the entire ovary and right tube were in the strangulated mass. Preoperatively it was noted that her secondary sex characteristics were poorly developed. Operation revealed a uterus little better than infantile. Would glandular therapy be indicated, and if so what type? If estrogen is given, will it depress the gonadotropic function of the anterior pituitary? Are there any satisfactory pituitary products available for such a case?

M.D., Connecticut.

ANSWER.—At the age this girl has reached, the amenorrhea is probably due to the infantilism. Delay in treatment increases the chances that the condition may become permanent, so treatment should be begun immediately. Thorough physical exami-

nation must be done in order to rule out vaginal occlusion, anemias, thyroid disease or any general debilitating disease that may be responsible for the amenorrhea. Should the examination reveal nothing abnormal, treatment with gonadotropic extract of pregnancy urine (antuitrin-S, antophysin, A. P. L., follutein) is indicated. This will stimulate the ovary to produce estrogen, which will act directly on the uterus to increase its size and develop the endometrium, thus providing the local conditions that lead to menstruation.

Council on Medical Education and Hospitals

ADDITIONAL HOSPITALS APPROVED

The Council on Medical Education and Hospitals of the American Medical Association has given its approval to the following hospitals since the publication of the last previous list in THE JOURNAL, August 28:

Hospitals Approved for Intern Training

Norwood Hospital, Birmingham, Ala.
Highland Sanitarium, Shreveport, La.
North Louisiana Sanitarium, Shreveport, La.
Tri-State Hospital, Shreveport, La.
Long Island Hospital, Boston.
Providence Hospital, Holyoke, Mass.
St. Mary's Hospital, Orange, N. J.
St. Mary's Hospital, Passaic, N. J.
Fairview Park Hospital, Cleveland.
St. Joseph's Hospital, Parkersburg, W. Va.
Presbyterian Hospital, San Juan, P. R.

Hospitals Approved for Residencies in Specialties

Anesthesia
Hartford Hospital, Hartford, Conn.
St. Mary's-Kahler Hospitals (Mayo Foundation), Rochester, Minn.
Flower-Fifth Avenue Hospital, New York City.

Medicine
St. Luke's Hospital, San Francisco.
Massachusetts Memorial Hospitals, Robert Dawson Evans Department of Clinical Research and Preventive Medicine, Boston.
De Paul Hospital, St. Louis.

Neurology
Gallinger Municipal Hospital, Washington, D. C.

Neuropsychiatry
Westboro State Hospital, Westboro, Mass.
Bishop Clarkson Memorial Hospital, Omaha.
Harding Sanitarium, Worthington, Ohio.
Danville State Hospital, Danville, Pa.

Obstetrics
Geo. F. Geisinger Memorial Hospital, Danville, Pa.

Obstetrics-Gynecology
Carney Hospital, Boston.
Flower-Fifth Avenue Hospital, New York City.

Orthopedics
Shriners Hospital for Crippled Children, Chicago.
St. Mary's Group of Hospitals, St. Louis.
Robert Packer Hospital, Sayre, Pa.
Children's Orthopedic Hospital, Seattle.

Otolaryngology
Flower-Fifth Avenue Hospital, New York City.
Temple University Hospital, Philadelphia.
Gill Memorial Eye, Ear and Throat Hospital, Roanoke, Va.

Pathology
Collis P. and Howard Huntington Memorial Hospital, Pasadena, Calif.
Children's Hospital, Washington, D. C.
Binghamton City Hospital, Binghamton, N. Y.
Temple University Hospital, Philadelphia.
Elizabeth Steel Magee Hospital, Pittsburgh.
Presbyterian Hospital, Pittsburgh.
Medical College of Virginia, Hospital Division, Richmond, Va.
State of Wisconsin General Hospital, Madison, Wis.

Pediatrics
Jewish Hospital, Philadelphia.

Radiology
Georgetown University Hospital, Washington, D. C.
Methodist Episcopal Hospital, Indianapolis.
Grace Hospital, Detroit.
Bronx Hospital, New York City.
Montefiore Hospital for Chronic Diseases, New York City (Diagnostic Service).
Temple University Hospital, Philadelphia.

Surgery
Georgetown University Hospital, Washington, D. C.
De Paul Hospital, St. Louis.
Rutherford Hospital, Rutherfordton, N. C.
Temple University Hospital, Philadelphia.
Children's Hospital, Pittsburgh.

Thoracic Surgery
Homer Folks Tuberculosis Hospital, Oneonta, N. Y.

Tuberculosis
Homer Folks Tuberculosis Hospital, Oneonta, N. Y.
Jefferson County Sanatorium, Watertown, N. Y.
State Tuberculosis Sanatorium, San Haven, N. D.
Germantown Dispensary and Hospital, Philadelphia.

Urology
St. Mary's Group of Hospitals, St. Louis.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, December 11, page 2011.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Examinations will be held in all centers where there is a Class A medical school and five or more candidates who wish to write the examination, Feb. 14-16, May 9-11 (limited to a few centers), June 20-22, and Sept. 12-14. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written examination for Group B applicants* will be held in various cities throughout the country April 16. *Applications due Feb. 15. Oral examinations for Group A and B applicants* will be held at San Francisco June 13-14. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: Examinations will be held in various centers of the United States and Canada, Feb. 14. Final date for filing applications is Jan. 1. Chairman, Dr. Walter L. Bierring, 406 Sixth Ave., Suite 1210, Des Moines, Iowa.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written examinations and review of case histories for Group B candidates* will be held in various cities of the United States and Canada, Feb. 5. *General oral, clinical and pathological examinations for all candidates (Groups A and B)* will be conducted in San Francisco, June 13-14. *Application for admission to Group A examinations must be on file before April 1.* Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: San Francisco, June 13. *All applications and case reports, in duplicate, must be filed at least sixty days before the date of examination.* Sec., Dr. John Green, 3720 Washington Blvd., St. Louis, Mo.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Los Angeles, Jan. 14-15. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: San Francisco, June 10-11. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 29-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave., N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: San Francisco, June 10-12. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

Vermont June Examination

Dr. W. Scott Nay, secretary, Vermont State Board of Medical Registration, reports the written examination held at Burlington, June 16-18, 1937. The examination covered 12 subjects and included 90 questions. An average of 75 per cent was required to pass. Twenty-six candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Tufts College Medical School		(1936)	82.2
University of Vermont College of Medicine		(1935) (1936)	88.1, 84.1, 86.1, (1937) 78.8, 80.7,* 84.4,* 85.1,* 86.1,* 86.1,* 86.1,* 87,* 87.2,* 87.8,* 88,* 88.1,* 88.1,* 88.8,* 88.8,* 89.3,* 89.4,* 89.6,* 89.6,* 89.9,* 90.7,* 97.3*

Ten physicians were licensed by endorsement from January 27 through October 12. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists		(1935)	N. B. M. Ex.
Georgetown University School of Medicine		(1934)	Mass., Penna.
Boston University School of Medicine		(1916) Mass., (1934)	N. B. M. Ex.
Hahnemann Med. College and Hospital of Philadelphia		(1934)	New Jersey
Univ. of Vermont College of Medicine		(1935), (1936, 3)	N. B. M. Ex.

* License withheld pending completion of internship.

Colorado October Report

Dr. Harvey W. Snyder, secretary, Colorado State Board of Medical Examiners, reports the written examination held at Denver, Oct. 6-8, 1937. The examination covered 8 subjects and included 165 questions. An average of 75 per cent was required to pass. Two candidates were examined, both of whom passed. Six physicians were licensed by endorsement on October 5. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Georgetown University School of Medicine		(1937)	84
University of Oklahoma School of Medicine		(1937)	84

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Northwestern University Medical School		(1933)	Minnesota
Creighton University School of Medicine		(1936)	Nebraska
University of Nebraska College of Medicine		(1933) (1936)	Maryland, Nebraska
Jefferson Medical College of Philadelphia		(1929)	U. S. Army
University of Wisconsin Medical School		(1929)	Utah

Book Notices

Textbook of Diagnostic Roentgenology. By Lewis J. Friedman, M.D., Director, Roentgen-Ray Department, Bellevue Hospital, New York. Cloth. Price, $10. Pp. 623, with 638 illustrations. New York & London: D. Appleton-Century Company, Incorporated, 1937.

The increasing utilization of the roentgen rays for diagnosis has brought about a need for more treatises on the subject. This book tends to fill the hiatus which exists between the small textbook for students and the large, detailed volume for the roentgenologist. There are three distinct classes of readers whose needs must be met: the undergraduate student, the general practitioner and the specialist in roentgen diagnosis. In a book of this size covering a subject whose scope is so broad, it is extremely difficult to satisfy all these groups. In this volume the student is given insufficiently exact descriptions of x-ray signs and differential diagnostic features. There is a glaring deficiency in the omission of any discussion of the indications for roentgen examination and of the relative value of the method. For the specialist in this field the treatment is too brief to be of great value. For the practicing physician who wishes quickly to find information on some feature of roentgen diagnosis, this book will prove to be most helpful. The author presents a short but clear summary of the fundamental physics of radiation. This, together with the inclusion of sections on x-ray technic, even including dark room procedures, will no doubt also appeal to the general practitioner. Normal appearances are well described and there is commendable attempt to present the common anatomic variations, particularly of the bones. Nevertheless, certain normal variants, such as the epiphysis of the tuberosity of the fifth metatarsal, the inferior accessory lobe of the lung and the prepyloric notch of the stomach, are omitted. The illustrations are generous and well reproduced. The line drawings are instructive and clarifying. There is an unfortunate tendency both in the text and in the illustrations to present the more unusual manifestations of disease, which may give the unwary reader a wrong impression. For the roentgenologist the illustrations are perfectly clear, but for the student or general practitioner more elaborate labeling and larger captions would be desirable. There are a number of specific criticisms, of which a few examples may be cited: The impression is created that the usual examination in cases of intestinal obstruction is by means of the barium meal, probably a harmful procedure. The use of the term "chronic myocarditis" is vague and misleading. The discussion of bone tumors, a most important subject, is much too brief. The observation of a peripheral triangle in lobar pneumonia can hardly be said to be a "rare observation." On the whole, however, the errors are not reprehensible. A bibliography is appended to each chapter. It would be well to point out that this was not intended, in any sense, to be complete. Otherwise a reader, unfamiliar with the roentgen literature, might be misled by the extreme paucity of references with regard to certain subjects. This volume covers a great deal of ground and for so short a book is unusually complete. It should be a valuable addition to the library of the general practitioner.

Analyse physique des calculs urinaires et biliaires. Par le Dr. E. Pillet. Paper. Price, 25 francs. Pp. 96, with 68 illustrations. Paris: Masson & Cie, 1937.

Dr. Pillet's small volume contains the results of his study of urinary and biliary calculi by physical means. He has subjected stones after comminution into minute particles to mineralogical examination, especially by means of the polarizing microscope. Crystallography, he states, is a science by which exact determinations can be made. These determinations should be made more widely known, as the use of a new method of examination brings with it new facts which may have an important value in the analysis of the subject of calculi formed in the human body. By the use of polarized light, each type of crystal found in urinary calculi has certain distinguishing physical characteristics which are constant. For example, oxalate stones are made up of small octahedrons and appear on section as lance shaped or as spheroliths depending on whether the urine is clear or contains blood. Calculi of uric acid have a lamellated structure quite different from the isolated crystal. Calculi of ammonium-magnesium phosphate are agglomerations of large flat crystals. Crystals are pyro-electric, which means that elevations of a fraction of a degree of temperature are sufficient to produce electrical potential at the extremities of the crystal. This type of investigation is interesting but highly technical and its value to the understanding of the pathogenesis of stone will necessitate more research and the critical application of the data furnished.

Charterhouse Rheumatism Clinic, Original Papers. Volume I. Cloth. Price, $5.25. Pp. 203, with illustrations. New York & London: Oxford University Press, 1937.

This book requires careful study. In order to appreciate it, one must have a keen interest in the subject and approach the material contained in the book with a very open mind. It is technical, the apparatus is expensive and the deductions have not been proved. The application of the pathogen selective cultures and sedimentation rate is made to various groups of arthritis and assists in a clearer understanding of the etiology, differential diagnosis, prognosis and therapeutics. The book contains an interesting clinical, radiologic and serologic correlation on spondylitis adolescens. Roentgenography makes the diagnosis on the basis of sacroiliac joint abnormalities long before the symptoms become manifest clinically. This early aid in diagnosis of disabling spinal affliction affords an advance in prophylaxis and therapy. There will be fewer undiagnosed or misdiagnosed early cases. Early treatment by roentgen irradiation, in dosage determined by sedimentation rate tests and clinical progress evaluation by sedimentation rate tests at regular intervals is recommended. The rheumatic patients are divided into ten classes, each of which is discussed individually. The book is divided into three parts: The Pathogen Selective Culture and Its Bearing on the Classification and Etiology of Chronic Rheumatic Disease, by H. Warren Crowe, The Differential Sedimentation Test, by Harry Coke, and Spondylitis Adolescens with Associated Pathological Changes in the Sacroiliac Joints, by S. Gilbert Scott. This is a book for specialists rather than for the general practitioner.

Infantile Paralysis and Cerebral Diplegia: Methods Used for the Restoration of Function. By Elizabeth Kenny. With a foreword by Herbert J. Wilkinson, Professor of Anatomy and Dean of the Faculty of Medicine, University of Queensland. Cloth. Price, 21s. Pp. 125, with 45 illustrations. Sydney, Australia: Angus & Robertson Limited, 1937.

This book contains discussions on infantile paralysis and spastic paralysis of infants. The author stresses the importance of restoration of function. In discussing infantile paralysis, she outlines the principles of treatment, apparatus used, treatment of complications, residual paralysis and muscle reeducation. Under the subject of spastic paralysis she discusses the condition as it is found in infants, the apparatus used in treatment, and the principles of treatment and exercises. There is a great deal of valuable information in the book and it is recommended to all those who are concerned with the diagnosis or treatment of persons afflicted with either disease or lesion. The treatment of infantile paralysis is based on the following five principles: (1) maintenance of a bright mental outlook, (2) maintenance of impulse, (3) hydrotherapy and remedial exercises, (4) maintenance of circulation, and (5) avoidance of the generally accepted methods of immobilization. There is an interesting foreword by H. J. Wilkinson, professor of anatomy and dean of the University of Queensland Faculty of Medicine.

Les péricystites. Par le Dr. P. Dominici. Paper. Pp. 334, with 31 illustrations. Paris: Jouve & Cie, Editeurs, 1937.

Dr. Dominici states in his preface that he has utilized the data included in the two extensive reviews on the subject of pericystitis which have appeared in the last twenty-five years: one by d'Aversenq in 1913 and the other by Paul Delbet in 1921; he has also added the many contributions in the literature, bringing it to date, and has included certain material which may have escaped the notice of the two authors cited. The volume is well printed and presents the subject in an orderly and comprehensive manner. It is remarkable for the excellence and clarity of the illustrations, many of which are original. Dominici's work is an important contribution to the literature on pericystitis chiefly on account of its completeness. The bibliography and extensive case reports culled from the litera-

ture permit ready reference to the various categories in which the author has divided his subject. Reference to many American authors is made, especially the work of Chute, Young, Beer and Culver. The book has its chief value as a reference work and affords an encyclopedic exposition of the subject.

The Technic of Local Anesthesia. By Arthur E. Hertzler, A.M., M.D., Ph.D., Professor of Surgery in the University of Kansas, Kansas City, Kansas. Sixth edition. Cloth. Price, $5. Pp. 284. St. Louis: C. V. Mosby Company, 1937.

This edition considers the few good anesthetics that are available for local anesthesia, the doses and the methods of their use, the combination of epinephrine with local anesthetics and the combination of local anesthetics and general anesthesia. There is a description of the syringes and needles recommended for this work and various other appliances that are conveniently used for this type of work. The various blocks are described on an anatomic basis, as for example in chapter IV, local anesthesia for operations on the scalp, the cranium and its contents, and in chapter V, local anesthesia for operations on the face, jaw and tongue. In the following chapters local anesthesia is described for operations on the ear and mastoid cells, for trifacial neuralgia and for operations on the fifth cranial nerve, cervical lymph nodes, buccal soft parts, thyroid gland, tonsils, larynx, trachea, mammary gland, thorax, lungs, spinal column and abdomen. Paravertebral and splanchnic anesthesia are dealt with in a chapter, as well as sacral and transsacral block anesthesia. There is a special chapter on spinal anesthesia written by Dr. Irene A. Koeneke, and this method is considered in considerable detail. There are further chapters on local anesthesia for operations on inguinal and femoral hernias and also for umbilical, linea alba and scar hernias, and for operations on the penis, scrotum, urethra, bladder, prostate gland, female organs and rectum, and upper and lower extremities. There is a short chapter on intravenous anesthesia with sodium amytal, which has not been used much clinically as a surgical anesthetic since 1930. The subject of preliminary medication is discussed briefly. This is a useful book for the general surgeon because the author's preference is infiltration of tissue to be incised, which is the most effective method for use by the general surgeon unless he also has been trained in regional methods of anesthesia. There are 142 excellent illustrations.

The Pneumonokonioses (Silicosis): Literature and Laws. Book III: International Abstracts, Extracts and Reviews of the Pneumonokonioses and Their Associated Diseases and Subjects. By George G. Davis, M.D., Associate Clinical Professor of Surgery, Rush Medical College, University of Chicago, Ella M. Salmonsen, Medical Reference Librarian, the John Crerar Library, Chicago, and Joseph L. Earlywine, Attorney at Law, Chicago. Cloth. Price, $8.50. Pp. 1,033. Chicago: Chicago Medical Press (Not Inc.), 1937.

Book III is similar in all respects to books I and II, which appeared respectively in 1934 and 1935. The present book embraces 701 abstracted articles related to dusty lung diseases, all of which appeared in 1935 and 1936. In addition, a small section is devoted to earlier publications overlooked in previous compilations. Such material, together with several indexes, make up part I of the present book and represents 900 pages. Part II of this volume presents the occupational disease laws of the United States and some mention of foreign countries. Taken in their entirety, these three books provide the best compilation in the English language of published materials related to dusty lung diseases. Book III is larger than either predecessor, which in part is due to the inclusion of large numbers of nonscientific discussions of dusty lung diseases, such as have appeared in lay papers. A few of these items represent abstracts of commercial promotional items in lay publications. The elimination of approximately one third of the abstracts would have made this valuable compilation even more valuable. It is observed that in the text of the entire series the term "silicosis" appears in parenthesis by the side of "the pneumonokonioses." Manifestly, silicosis is not a synonym of "the pneumonokonioses," although silicosis is one of the pneumoconioses. The previous publications in this series have been given favorable reception by physicians, attorneys, engineers and industrial hygienists. There is no reason to believe that this book will prove any less useful or any less popular, even though it appears at a time when dramatic concern in silicosis, so prevalent a few years ago, is now distinctly on the wane.

Soubor prací věnovaných Profesoru V. Libenskému na počest jeho šedesátých narozenin. Recueil de travaux dédiés au Prof. V. Libenský en l'honneur de son soixantième anniversaire. Časopis lékařů českých, Number 22, June 7, 1937. Cloth. Pp. 277, with illustrations. Prague: Société Tchécoslovaque de Cardiologie, 1937.

This collection of articles in honor of Prof. Vaclav Libensky's sixtieth anniversary is presented in book form, divided into two parts. The first part contains sixty-two pages of articles contributed in French and Italian by various foreign authors; the second and larger part presents articles contributed in Czechoslovakian by native authors, each having a French or English summary. The articles are mostly on subjects of internal medicine, the circulatory system being given the preference. The articles are rather short, but all are interesting and written by well known authors.

The Kinesiology of Corrective Exercise. By Gertrude Hawley, M.A., Assistant Director, Women's Gymnasium, Stanford University, California. Cloth. Price, $2.75. Pp. 268, with 107 illustrations. Philadelphia: Lea & Febiger, 1937.

Active exercise, because of its wide applicability and its importance in developing the body to the highest possible mechanical efficiency, probably should be given first place in the many agents used in physical therapy. This small volume, which is intended for students, teachers and physical therapists specializing in the field of corrective exercise, is a practical textbook on kinesiology. The exercise treatment of infantile paralysis, spastic paralysis and fractures is not discussed, but it does give exercises suitable for use in any corrective or remedial physical education department where a reasonable amount of personal supervision can be given by the instructor. It can be recommended to teachers interested in this branch of physical education.

Quantitative Pharmaceutical Chemistry Containing Theory and Practice of Quantitative Analysis Applied to Pharmacy. By Glenn L. Jenkins, Ph.D., Professor of Pharmaceutical Chemistry, College of Pharmacy, University of Minnesota, and Andrew G. DuMez, Ph.D., Professor of Pharmacy and Dean of the School of Pharmacy, University of Maryland. Second edition. Cloth. Price, $3.50. Pp. 466, with 67 illustrations. New York & London: McGraw-Hill Book Company, Inc., 1937.

This book covers both general and physical methods used in official pharmaceutic analysis as directed by the United States Pharmacopeia and the National Formulary and aims to develop a logical explanation for the various steps in the analysis as well as presenting questions and problems which are intended to develop the student's reasoning capacity. The first chapter is an excellent introduction to general chemical analytical methods, including simple statistical presentation of results and presentations of such calculations as probable error, gravimetric methods applied to official substances, volumetric analysis, alkalimetry, acidimetry, precipitation methods, oxidation and reduction methods and gasometric methods. Part II is devoted to an exposition of physicochemical methods used in official assaying. In part III, special methods such as ash and moisture determinations, extractive and crude fiber content and analyses of drugs for proximate principles are taken up. This book bears the stamp of many years of experience in teaching and should be a welcome laboratory manual, most especially for students in colleges of pharmacy.

Aids to Physiology. By Henry Dryerre, Ph.D., M.R.C.S., L.R.C.P., Professor of Physiology, Royal (Dick) Veterinary College, Edinburgh. Second edition. Cloth. Price, $1.25. Pp. 295, with 63 illustrations. Baltimore: William Wood & Company, 1937.

A book for the rapid reviewing of facts in a science is occasionally an aid to a candidate for an examination but is ordinarily useless for study. This book is reasonably accurate and is well composed. It is essentially a dictionary arranged under the conventional headings of the physiologic and anatomic subdivisions of the body. All aspects of the subject are covered, but in brief and dogmatic form. One defect in such a work is that the reader has no way of knowing which of the statements are well substantiated and which are not. In physiology today many qualifications must be made and questions left unanswered because of inadequate knowledge. It would be highly undesirable to recommend this work as a student's textbook.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Failure to Observe Symptoms of Eclampsia.—The plaintiff, as administrator of the estate of his deceased wife, sued the Columbia Clinic, Inc., and Dr. Hackett, an employee of the clinic, attributing the death of his wife to their negligence. The jury returned a verdict against the clinic but for Dr. Hackett, and the clinic appealed to the Supreme Court of Washington.

The Columbia Clinic, Inc., was a corporation operating a hospital in the city of Longview with the usual staff of physicians, nurses and attendants. The plaintiff, an employee of a company operating in the vicinity, had a "family contract" for the medical care and hospital treatment of the members of his family by the Columbia Clinic, Inc. April 21, 1934, he and his wife went to the hospital, saw Dr. Hackett and advised him that the plaintiff's wife was pregnant and expected to be confined in about a month. Dr. Hackett apparently made the usual examination and inquired into the facts of the case and the family history of the expectant mother. He gave directions as to how the patient should conduct herself and asked her to bring in for examination, at intervals, specimens of her urine. According to the physician's testimony, the condition of the patient at that time was normal. Samples of urine were brought in on two later occasions which Dr. Hackett testified indicated a normal condition. The patient was taken to the hospital about 5 o'clock on the morning of May 28 and placed in the care of a nurse then in charge, and Dr. Hackett was notified of her arrival. He did not go to the hospital until about 8:30 and did not then see the patient. He did, on his arrival at the hospital, look at the hospital chart, which, he testified, showed that the case was progressing with normal labor. Later, Dr. Hackett found that his services as a surgeon were required in a case involving severe injuries and asked another member of the hospital staff, a Dr. Clark, who specialized in obstetric cases, to take care of the patient. Dr. Clark did not see the patient until 11:45 a. m. He then made what the record refers to as a cursory examination and concluded that the patient was normal and that the case was proceeding normally. At 1:40 p. m. Dr. Clark again saw the patient, made a further examination and again concluded that everything was progressing normally. At that time he expected delivery within two hours. About 2 o'clock the patient suffered a convulsion and Dr. Clark was immediately called and found her in a comatose condition. She was rushed to the delivery room and the baby was delivered within fifteen minutes by the use of forceps. The patient was then taken to the maternity ward and put to bed. The nurse there in charge was informed of what had taken place and was told to watch the patient and to advise Dr. Clark of developments.

Dr. Clark saw the patient later in the afternoon and, as he testified, "talked to her, asked her how she was, turned around and came out again." Dr. Hackett looked in to see the patient in midafternoon and both Dr. Hackett and Dr. Clark visited her at about 6 p. m. At neither time, according to their testimony, did either see anything wrong and no treatment was ordered except that which is given in a normal case. Beginning about 7 o'clock in the evening, the patient again had convulsions and from that point on it seems to be conceded that she received proper treatment, notwithstanding which in a few hours she died. It was the plaintiff's theory that certain symptoms were present when Dr. Hackett first examined the patient which indicated at that time the presence, or the prospective presence, of eclampsia. Lay witnesses testified that such symptoms were then present, but Dr. Hackett testified to the contrary. Medical testimony was introduced to the effect that eclampsia being present, or there being present the symptoms from which it may be expected that it will develop, there is a known treatment which should be at once applied and which, when applied, will greatly lessen the probability of a fatal ending. No such treatment was given to the patient until after she again had convulsions at 7 o'clock in the evening, after the birth of her child.

Dr. Hackett did not treat the patient after she came to the hospital but turned the case over to Dr. Clark. There was therefore, the court said, a wide open opportunity for the jury to find that Dr. Hackett was not negligent but that the nurse who received the patient at the hospital was negligent in not discovering the symptoms of eclampsia and recording them on the hospital chart so that Dr. Hackett, when he read the chart, might have ordered the proper and necessary treatment. The symptoms of eclampsia are such, the court said, as should be observed by a nurse even though she might not know what was indicated thereby. Furthermore, the jury might have found that Dr. Clark was negligent in one or more of several ways: (1) by his failure to see the patient until 11:45 a. m., more than six hours after her arrival at the hospital and at least two or three hours after the case had been turned over to him by Dr. Hackett; (2) by not then discovering the symptoms of eclampsia and ordering the proper treatment; and (3) by his failure to discover the symptoms at the time of the delivery of the baby or subsequently during the afternoon and then ordering a treatment which would probably have prevented the development of eclampsia and the return of the convulsions. There was evidence, also, from which the jury could have found that the nurse in the maternity ward was negligent in not keeping a closer watch over the patient during the hours following delivery and in not observing and calling attention to the symptoms then present. It seems clear, the court said, from these facts that the jury could, as it did, exonerate Dr. Hackett and yet, by finding negligence on the part of some other employee of the clinic, render a verdict against it. The charge and the proof was such as to permit the jury to find any one or more of four employees to be guilty and a verdict in favor of the employee who was made a party is not a finding that another or other employees, not parties, were not guilty.

The judgment of the trial court, therefore, against the clinic was affirmed.—*Hansch v. Hackett et al. (Wash.), 66 P. (2d) 1129.*

Workmen's Compensation Acts: Diabetic Gangrene Precipitated by Trauma.—The petitioner, a night watchman at the building of the defendant trust company, was afflicted with diabetes, though apparently he did not know it at the time of the accident. While he was making one of his rounds he stubbed a toe on which there was a callous area against a chair. He at once felt acute pain in the toe, which increased during the course of the night. The following morning he was taken to a hospital dispensary and reported to the physician there that he had stubbed his toe against a chair. Two days later when he returned to the hospital diabetes was suspected and an examination of the urine confirmed that suspicion. Signs of incipient gangrene were then observed. From this point, the case progressed to an amputation of the leg below the knee. The petitioner instituted proceedings under the workmen's compensation act of New Jersey and obtained an award. This award was affirmed by the court of common pleas, Passaic County and the trust company brought certiorari to the supreme court of New Jersey.

In the opinion of the supreme court, the evidence tended to show that an accident in the course of employment and arising out of it was a substantial contributing cause of the disability sustained by the petitioner. The inference was entirely reasonable from the testimony that the accident incited a tendency to gangrene existing because of the diabetic condition of the petitioner. The award was therefore affirmed.—*Cahill v. Franklin Trust Co. (N. J.), 191 A. 748.*

Society Proceedings

COMING MEETINGS

American Academy of Orthopedic Surgeons, Los Angeles, Jan. 16-20. Dr. Carl E. Badgley, 1313 East Ann St., Ann Arbor, Mich., Secretary.

American Student Health Association, Chicago, Dec. 30-31. Miss Ruth E. Boynton, University of Minnesota Medical School, Minneapolis, Secretary.

Puerto Rico, Medical Association of, Santurce, Dec. 17-19. D. M. Pinero, Avenue Fernandez Juncos, 19, Santurce, Secretary.

Society of American Bacteriologists, Washington, D. C., Dec. 28-30. Dr. I. L. Baldwin, College of Agriculture, University of Wisconsin, Madison, Wis., Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers in continental United States and Canada for a period of three days. Periodicals are available from 1927 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them. Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

54: 973-1210 (Nov.) 1937

Comparative Study of Immunization. E. B. Shaw, San Francisco.—p. 973.

Present Status of Preventive Inoculations Against Whooping Cough. L. Sauer, Evanston, Ill.—p. 979.

Acute Anterior Poliomyelitis in New York in 1935: Review of 686 Cases. A. E. Fischer and M. Stillerman, New York.—p. 984.

*Blood Sugar in Diabetes in Children. A. H. Kantrow, Brooklyn, and J. D. Boyd, Iowa City.—p. 1005.

Sympathetic Innervation of External Sphincter of Human Bladder. P. C. Bucy, C. Huggins and D. N. Buchanan, Chicago.—p. 1012.

*New Tuberculin Patch Test. H. Vollmer, New York, and Esther W. Goldberger, Staten Island, N. Y.—p. 1019.

Mineral Composition of Bone and Cartilage of Human Fetus. W. W. Swanson and L. V. Iob, Chicago.—p. 1025.

Respiratory Metabolism in Infancy and in Childhood: XX. Nitrogen Metabolism in Premature Infants—Comparative Studies of Human Milk and Cow's Milk. H. H. Gordon, S. Z. Levine, M. A. Wheatley and E. Marples, New York.—p. 1030.

Circulatory Collapse in Diphtheria. C. W. Edmunds, Ann Arbor, Mich.—p. 1066.

Blood Sugar in Diabetes in Children.—Kantrow and Boyd investigated the nocturnal fluctuations of the blood sugar level of diabetic children, the blood sugar level in the early morning hours after awakening but before the ingestion of food or the administration of insulin, and the response to standardized doses of insulin unaccompanied by food. In all, 299 separate tests were completed, 207 with diabetic and ninety-two with nondiabetic subjects. Since the blood sugar level of the diabetic subject reacts at a different tempo from that of the nondiabetic subject, an insulin tolerance test may prove as valuable a means of diagnosing the presence of diabetes as is the dextrose tolerance test. The hyperglycemia of hyperthyroidism may be distinguished from that of diabetes in this manner. The test as performed consists of the administration of one-fourth unit of insulin per kilogram of body weight and the determination of the blood sugar level before and at four half-hour intervals subsequently. The maximal reduction in the nondiabetic subject is observed within the first half hour, whereas in the diabetic subject the fall is prolonged into the second or third half hour or longer. This peculiarity of response seems inherent in the diabetic organism and is not determined by the initial blood sugar level, nor is there evidence that the nature of the response is altered by treatment of the disease.

New Tuberculin Patch Test.—Vollmer and Goldberger describe a new patch test, which has the advantage of simplicity over other tuberculin tests. Thin filter paper is saturated with tuberculin, suspended in the air in a room free from dust and allowed to dry. This saturated filter paper when dry can be kept indefinitely. The paper is cut into 0.8 cm. squares and placed on adhesive tape with forceps. Three types of plasters are prepared in this way: (1) plasters equipped with old tuberculin, (2) plasters containing old tuberculin and bouillon control and (3) plasters containing old tuberculin, control material and bovine tuberculin. The distance between these squares must be at least 1 cm. When more than one square is used, each square is distinguished by a specific letter on the back of the plaster. The adhesive side of the plaster can be protected with stiff gauze. By the natural moisture of the skin this tuberculin is liquefied sufficiently to cause a cutaneous reaction. In spite of this dilution by moisture, the tuberculin remains sufficiently concentrated to cause a reliable cutaneous reaction. The control square does not cause an inflammatory reaction. However, a sensitive skin may occasionally give a nonspecific irritative reaction caused by the adhesive plaster. Therefore it is always best to use a control square. In carrying out the test the skin is cleansed with ether or benzene and the plaster, from which the gauze has been removed, is placed securely on the skin. After twenty-four hours the reaction was read. The results were more reliable when the plaster was left on for forty-eight hours. The reaction may be read immediately after removal or twenty-four hours later, at which time possible nonspecific skin reactions have disappeared and the tuberculin reaction is intensified. When positive, the reaction appears as a sharply defined, indurated, reddened square, with lichenoid, follicular elevations on the skin. Reactions are usually clearcut when the plaster is put lengthwise on the sternum or transversely over the upper edge of the trapezius muscle. This eliminates spreading of the tuberculin as the result of folds in the skin. The reliability of the test can be seen in that 187 of 209 tuberculous children, or 89.5 per cent, showed a conformity between the results of the Pirquet test and those of the present patch test. The results that did not correspond were in fifteen children who showed a negative reaction to the Pirquet test and a positive reaction to the patch test and in seven children who showed a positive reaction to the Pirquet test and a negative reaction to the patch test. The fundamental principle of the tuberculin patch test with saturated filter paper proved, after modification, to be fit also for an allergy patch test.

American Journal of Medical Sciences, Philadelphia

194: 597-748 (Nov.) 1937

Roentgen Therapy of Active Rheumatic Heart Disease: Summary of Eleven Years' Experience. R. L. Levy and R. Golden, New York.—p. 597.

Clinical Observations on Dynamics of Ventricular Systole: IV. Pulsus Alternans. L. N. Katz, Chicago, and H. S. Feil, Cleveland.—p. 601.

Suppurative Pleuritis Complicating Pulmonary Infarction in Congestive Heart Failure. I. Steinberg, E. Clark and C. E. de la Chapelle, New York.—p. 610.

Observations on Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: VI. Site of Interaction of Food (Extrinsic) and Gastric (Intrinsic) Factors; Failure of In Vitro Incubation to Produce a Thermostable Hematopoietic Principle. W. B. Castle, C. W. Heath, M. B. Strauss and R. W. Heinle, Boston.—p. 618.

Etiology and Treatment of Idiopathic Hypochromic Anemia. W. M. Fowler and Adelaide P. Barer, Iowa City.—p. 625.

*Studies on Anemia of Chronic Glomerulonephritis and Its Relationship to Gastric Acidity. S. R. Townsend, E. Massie and R. H. Lyons, Boston.—p. 636.

*Deficiency Syndromes Associated with Chronic Alcoholism: Clinical Study. J. Romano, Denver.—p. 645.

Case Finding in Tuberculosis, an Adult Problem. H. R. Edwards, New York.—p. 652.

Diagnostic Importance of Tongue in Internal Medicine. B. I. Comroe, Philadelphia.—p. 661.

Loss of Body Heat and Disease. W. Landauer, Storrs, Conn.—p. 667.

Calcium Ion Concentration of Serum in Allergic Diseases. W. B. Sherman and Mary Glidden, New York.—p. 674.

Survey of Undulant Fever and Bang's Disease in the United States. L. Gershenfeld and D. C. A. Butts, Philadelphia.—p. 678.

Convalescence, with Especial Reference to the Philadelphia Area. J. H. Cloud, Ardmore, Pa.—p. 684.

Causative Factors in Production of Laënnec's Cirrhosis, with Especial Reference to Syphilis. G. A. Schumacher, Philadelphia.—p. 693.

Leiomyoma of Small Intestine: Report of Case with Fatal Hemorrhage. O. N. Smith, Philadelphia.—p. 700.

Studies of Myohemoglobin at High Altitudes. A. Hurtado, A. Rotta, C. Merino and J. Pons, Lima, Peru.—p. 708.

Relation of Anemia of Chronic Glomerulonephritis to Gastric Acidity.—Since previous studies on the anemia of nephritis have failed to utilize more accurate methods, Townsend and his associates felt that the application of the hematologic technic to their patients would enable them to classify their anemias more definitely, might give some clue toward the recognition of the fundamental defect present in the anemia of nephritis and possibly suggest a more efficacious treatment, and that an assessment of the gastric acidity might disclose some correlation between the developing anemia, nitrogen retention and diminishing gastric acidity. The refractory nature of the anemia to iron therapy has always been a puzzling one and suggests that such medication may fail because of a disturbed gastric secretion. Their observations on the character of the red blood cell in the anemia of chronic glomerulonephritis permit them to classify the anemia as one of the normocytic variety; but in some of the individual cases the

hemoglobin content is slightly lower than that commonly associated with this type of anemia. A deficient supply of erythrocytic building material might be considered the possible explanation for this type of picture. It is common knowledge that the anemia of chronic glomerulonephritis does not respond to iron, and the slightly lower hemoglobin found in the individual red cell is probably of significance and compatible with the thought that the anemia is due to a deficiency of blood cell forming material. Studies on the gastric acidity tend to support this view. The most important features in the anemia of chronic glomerulonephritis is the diminished or absent hydrochloric acid in the gastric secretion, and this diminution must play an important part in the improper digestive processes and improper absorption of food and iron. The investigations indicate that there is a correlation between the decreased renal function, the development of a normocytic anemia and the development of a low to absent secretion of free hydrochloric acid. The low gastric acidity, by interfering with the proper metabolism of ingested food and the absorption of iron, indirectly produces a deficiency of "building material" for sufficient red blood cell formation and the production of hemoglobin.

Deficiency Syndromes Associated with Chronic Alcoholism. — Physical, neurologic and psychiatric examinations were carried out in 131 cases of chronic alcoholism. Romano paid particular attention to the dietary history, presence or absence of polyneuritis, anemia and clinical response to vitamin B therapy. The age period between 30 and 50 contained more than 64 per cent of the 131 patients; sixteen were women. Eleven of the women and sixty-four of the men had some qualitative inadequacy in their diets for varying periods previous to admission. Of the seventy-seven patients who showed evidence of some form of neuritis, sixty-one gave a history of inadequate diets. Ten of the female patients and sixty-seven of the male patients suffered from some degree of peripheral neural involvement. Eleven of the women and sixty-four of the men suffered from some degree of anemia, although fifty-six of the total number of patients with some degree of anemia had only mild involvement. Of the nineteen patients who had moderate or severe anemia, six had macrocytosis as revealed by increased cell diameter and volume index. Iron and ammonium citrate in large daily doses (from 4 to 8 Gm.) together with parenteral liver were successful in treating the anemias. Every patient with mild, moderate or severe peripheral neural involvement was placed on a high caloric, high vitamin diet (from 4,000 to 5,000 calories daily) the quantity of protein obtained from lean meat being increased and the carbohydrate decreased. This diet was supplemented with dried brewers' yeast tablets (4 Gm. daily), wheat germ preparations (from 30 to 60 Gm. daily) and either vitamin B_1 or preparations of liver given parenterally in daily doses. In addition to this, fresh orange or tomato juice together with various preparations of cod or halibut liver oil were given. Of the seventy-seven patients with neuritis, five failed to respond to vitamin therapy, forty-seven showed partial improvement and twenty-five showed complete improvement with specific therapy during their period of hospitalization (average 24.67 days).

American Journal of Orthopsychiatry, Menasha, Wis.

7: 441-550 (Oct.) 1937

Study of Basal Age with Reference to Its Meaning for School Adjustment. I. S. Wile and Rose Davis, New York.—p. 441.

Fairy Tales, Lilliputian Dreams and Neurosis. S. Lorand, New York.—p. 456.

A Case of Delinquency. P. Sloane and Vivian Lane, Allentown, Pa.—p. 465.

Treatment Possibilities Offered by the Summer Camp as Supplement to the Child Guidance Clinic. J. Galkin, New York.—p. 474.

Emotional and Biologic Factors Involved in Learning Processes. E. Liss, New York.—p. 483.

Casework with Adolescents Who Have Run Afoul of the Law. Susan Burlingham, Philadelphia.—p. 489.

Reaction of Children to Sexual Relations with Adults. Lauretta Bender and A. Blau, New York.—p. 500.

Effect of Benzedrine Sulfate on Children Taking the New Stanford Achievement Test. M. Molitch and J. P. Sullivan, Jamesburg, N. J.—p. 519.

The Use of the Play Situation as an Aid to Diagnosis: Case Report. P. Holmer, Reading, Pa.—p. 523.

Sociologic and Psychiatric Interview Compared. W. C. Reckless and L. S. Selling, Detroit.—p. 532.

American Journal of Physiology, Baltimore

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Blood Sugar Recovery from Insulin Hypoglycemia After Section of Splanchnic Nerves. B. N. Berg and T. F. Zucker, with assistance of H. B. Colman and Helen Blodgett, New York.—p. 435.

Epinephrine Output from Adrenal Glands in Experimental Diabetes. J. M. Rogoff and E. Nola Nixon, Chicago.—p. 440.

Significance of Subnormal Respiratory Quotient Values Induced by Controlled Feeding in the Rat. N. Werthessen, Cambridge, Mass.—p. 458.

Ovarian Weight Responses to Menopause Urine Injections in Normal, Hypophysectomized and Hypophysectomized Thyroxine-Treated Immature Rats. H. H. Tyndale and L. Levin, New York.—p. 486.

Reversible Inhibition of Muscle Glycolysis. C. L. Gemmill and L. Hellerman, Baltimore.—p. 522.

Insulin and Gastric Motility. J. Lalich, W. B. Youmans and W. J. Meek, Madison, Wis.—p. 554.

*Electrencephalogram of Schizophrenics During Insulin Hypoglycemia and Recovery. H. Hoagland, M. A. Rubin and D. E. Cameron, Worcester, Mass.—p. 559.

Analysis of Chronotropic Function of Cardiac Vagus Nerves. A. S. Gilson Jr., St. Louis.—p. 571.

Respiratory Quotient and Carbohydrate Metabolism Following Ingestion of Glucose and of Fructose as Affected by Exercise Taken Immediately and Thirty Minutes After Ingestion. G. Bachmann, J. Haldi, W. Wynn and C. Ensor, Emory University, Ga.—p. 579.

Experimental Analysis of Centripetal Visceral Pathways Based on Visceropannicular Reflex. D. M. Ashkenaz, Philadelphia.—p. 587.

Effect of Thyreotropic Hormone Combined with Small Amounts of Iodine on Function of Thyroid Gland. Evelyn M. Anderson and H. M. Evans, Berkeley and San Francisco.—p. 597.

Acid Inhibition and Cephalic (Psychic) Phase of Gastric Secretion. C. M. Wilhelmj, H. H. McCarthy and F. C. Hill, Omaha.—p. 619.

Electrencephalogram in Schizophrenia During Insulin Hypoglycemia.—Hoagland and his associates made electrencephalographic records during thirty-five insulin treatments of six schizophrenic patients. Electrical brain waves after large doses of insulin show a progressive decline in the frequency of the alpha wave (Berger rhythm) of some 40 per cent, which parallels with a time lag of some minutes (about thirty) the declining blood sugar curve. Sugar injected during coma restores the frequency along a smooth curve. The present data, along with other evidence, are in accordance with the view that alpha frequencies are directly proportional to the rate of carbohydrate metabolism of the cortical cells producing the rhythm.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

38: 533-676 (Oct.) 1937

Roentgenologic Aspects of Chronic Gastritis: Critical Analysis. A. Ansprenger and B. R. Kirklin, Rochester, Minn.—p. 533.

Exploration of Biliary Ducts by Cholangiography During and Following Operation. H. B. Hunt, N. F. Hicken and R. R. Best, Omaha.—p. 542.

*A Safe Method for the Roentgen Demonstration of Bleeding Duodenal Ulcers. A. O. Hampton, Boston.—p. 565.

Roentgenographic Demonstration of Method of Speech in Cases of Complete Laryngectomy. G. R. Brighton and W. H. Boone, New York.—p. 571.

Lesions of the Diaphragm. E. L. Jenkinson and E. W. Roberts, Chicago.—p. 584.

Roentgenologic Considerations in Infant Mastoiditis. C. F. Crain, Corpus Christi, Texas.—p. 592.

Urographic Pyelolymphatic Backflow. M. F. Campbell, New York, and V. B. Seidler, Montclair, N. J.—p. 602.

Pelvimetry by Stereoroentgenometry. C. R. Johnson, Whittier, Calif.—p. 607.

*Treatment of Roentgen Sickness with Synthetic Vitamin B_1 Hydrochloride: Preliminary Report. C. L. Martin and W. H. Moursund Jr., Dallas, Texas.—p. 620.

A Portable Low Intensity High Voltage Roentgen Therapy Unit. I. I. Kaplan and S. Rubenfeld, New York.—p. 625.

The Educational Advantages of the Tumor Clinic. G. M. Dorrance, Philadelphia.—p. 636.

Roentgen Demonstration of Bleeding Duodenal Ulcers.—Hampton describes a method for the demonstration of dangerously bleeding duodenal ulcers. It permits profile, relief and double contrast examination of the posterior wall of the stomach, the pyloric valve and the posterior wall of the duodenum. The entire examination is done with the patient in a horizontal position when compression or palpation is contraindicated or impossible. The equipment necessary for the examination consists of a horizontal roentgenoscope and a quick change-over switch, which will allow the taking of films rapidly during roentgenoscopic observations. The patient should be shifted from the hospital truck to the roentgenoscopic table on a stretcher. The barium suspension must be prepared carefully. An electrical mixer is recommended. There are certain already prepared barium mixtures on the market which can be used.

The author uses by volume 4 ounces of plain barium sulfate, 3 ounces of water and 1 teaspoonful of liquid petrolatum with agar. More barium can be added by the addition of liquid petrolatum with agar without increasing the viscosity of the mixture. The mixture should be freshly made and of about the consistency .. heavy cream. After the patient has ingested the barium meal as he lies on his back, he is rotated toward his right side and allowed to remain in this position under roentgenoscopic observation until the first part of the duodenum has filled and emptied two or three times. Then when the duodenum is completely filled he is promptly returned to the face-up position and rotated more to the left side until the pyloric valve and first portion of the duodenum are seen in profile. Roentgenograms are taken with the roentgenoscopic tube immediately while the duodenum is still filled and when abnormalities are noted, but it is when the patient is lying face up, slightly rotated to the left, that the best examination of the duodenum is obtained. The inner relief of the posterior wall of the duodenum can be visualized by taking films after the duodenum has emptied. Thick barium will adhere to the duodenal mucosa and by the force of gravity will remain in such ulcerous craters as are present. The double contrast examination is then done. There is usually a gas bubble present in the stomach, but if there isn't the patient should be instructed to swallow four or five times. When the fundus gas bubble is in the antrum, pyloric valve and duodenum films are taken for double contrast examination. This allows a study of the gastric and duodenal relief exactly as is obtained by the double contrast enema.

Treatment of X-Ray Sickness with Vitamin B_1 Hydrochloride. — Martin and Moursund observed that in animals deprived of vitamin B_1 symptoms similar to those seen in x-ray intoxication develop. The four major points of similarity are loss of appetite, changes in intestinal motility and tonus, changes in the mucous membranes of the gastro-intestinal tract and alteration of the sugar metabolism. For more than six months, patients with x-ray sickness have been treated with oral or intramuscular injection of vitamin B_1 hydrochloride and the clinical results were most striking. A series of animal (guinea pig) experiments has been carried out in an effort to establish a sound basis for the use of this preparation. The experimental results support the use of vitamin B_1 in the treatment of x-ray sickness.

American Journal of Surgery, New York

38: 227-458 (Nov.) 1937

Malignancies of Rectum and Rectosigmoid. C. G. Heyd, New York.—p. 230.
*New Method in the Use of Radon Gold Seeds. F. Hames, New York.—p. 235.
Postoperative Complications Following Suprapubic Prostatectomy and Their Prevention. M. Muschat, Philadelphia.—p. 239.
Minor Enlargement of Prostate. E. W. Hirsch, Chicago.—p. 248.
Roentgen Diagnosis of Diaphragmatic Hernia. A. S. Unger and M. H. Poppel, New York.—p. 251.
A Method for Reducing the Postoperative Morbidity of Cholecystectomy. T. B. Noble Jr., Indianapolis.—p. 259.
Postoperative Study of Peptic Ulcer. B. M. Bernstein, D. Diamond and J. Zaslow, Brooklyn.—p. 266.
Acute Appendicitis in Children. F. Angel, E. Angel and A. Kizinski, Franklin, N. C.—p. 268.
Hyperparathyroidism: Diagnosis and Treatment. J. E. Jacobs and J. D. Bisgard, Omaha.—p. 272.
Id.: Collected Cases. J. E. Jacobs and J. D. Bisgard, Omaha.—p. 286.
Surgical Treatment of Pendulous Hypertrophic Breast. P. Posse, Buenos Aires, Argentina.—p. 293.
*Ingrown Toenail: Clinical Study. C. J. Heifetz, St. Louis.—p. 298.
Venous Thrombosis in Lower Limbs: Its Relation to Pulmonary Embolism. J. Homans, Boston.—p. 316.
Osteomyelitis in Compound Fractures. R. H. Kennedy, New York.—p. 327.
Reconstruction Operation for Comminuted Fracture of Upper Third of the Ulna. L. V. Rush and H. L. Rush, Meridian, Miss.—p. 332.
Treatment of Distention by Continuous Duodenal Suction. M. S. Weinberg, New York.—p. 334.
*Rectal Evipal as Complete Anesthesia: Clinical Observations on 200 Cases: Preliminary Report. H. Hogan, New York.—p. 340.
Antiseptics and Wound Healing. W. W. Sager, E. B. Vedder and C. Rosenberg, Washington, D. C.—p. 348.
Intestinal Resection by a Single Clamp Method. N. N. Ssamarin, Leningrad, U. S. S. R.—p. 351.

New Method in Use of Radon Gold Seeds.—To overcome the limited mobility of the treated part during the use of needles containing radon or radium, the inability of disposing of saliva and consequent pulmonary complications when platinum needles are used in and around the oral cavity and the possible inaccurate placement of platinum needles, Hames outlines a radon suture method which consists in the placing of radon seeds within the lumen of a specially made silk carrier. The spacing between openings into which the radon is placed can be varied at will. Those that he used in his cases were all placed 1 cm. apart. The usual filtration of 0.3 mm. of gold has been employed, but this may be increased as desired. After the radon seeds are placed in the body of the woven silk material, they are permanently sealed in place by the closure of the woven structure and also by a plastic substance containing carmine as an indicator of the area in the suture in which the radon is situated. The spaces between the implants are filled with silk, so that there is a uniform diameter of the suture material throughout its length. On one end of the suture is a small, permanently attached metal collar. The distal end of this collar is threaded to receive the needle of whatever type may be desired. The needle is threaded at one end in order to permit its being screwed into the metal collar. The needle is passed through the tissue around or beneath the area to be treated and the proper placement of the suture is guided by the red markings indicating the point of radon activity. After the suture is so placed, a glass bead is threaded over either end and brought to rest against the tissue. Above this bead a lead shot is fixed to hold the material in place until such time as its removal is desired. In removing the device the suture is cut below the fixed bead and withdrawn in a manner similar to that used in removing an ordinary cutaneous suture or capillary drain. When it is unnecessary or impossible to use a needle, the radon loaded suture may be packed into the cavity —as the antrum or the uterus—after being attached to the usual packing gauze, and its removal readily accomplished by removing the packing. The method provides a means of using radon by the average surgeon, who may be distant from the source of supply of radium and radon.

Ingrown Toenail.—Heifetz summarizes the present status of the subject of ingrown toenail and presents a routine of treatment which he has used for several years. The main underlying causes of ingrown toenail are ill fitting footwear and improper cutting of the nails. The use of cotton packing, if properly applied, is one of the simplest effective means of conservative treatment. Radical operation is simplified in the method of Winograd, which the author uses with modifications in certain cases. From three to five days before operation, depending on the infection present, the patient soaks and cleanses his foot in warm water (110 F.) for an hour twice a day. The operative field is made bloodless by the application of a tourniquet. From 3 to 4 cc. of a 2 per cent solution of procaine hydrochloride is injected on each side of the toe at different sites. An incision three-eighths inch long is made in the eponychium and proximal wall of the nail, extending slightly diagonally laterally from a point on the nail corresponding to the line on which the nail will presently be excised. This is made deep enough to strike the root of the nail. Medial and lateral flaps are dissected along this line so as to expose at least the lateral third of the root of the nail on that side. The lateral flap should also include sufficient tissue so as to expose the embedded edge of the nail. A small thin flat spatula similar to the Bollenger-Hajek nasal elevator is inserted beneath the free border to the nail between the plate and the bed of the nail along the line where the nail is to be cut, and, hugging the undersurface of the nail, is pushed proximally until it emerges in the incision proximal to the root of the nail. This spatula is then worked laterally until it lifts the involved portion of the nail from its bed. The freed involved portion of the nail is excised along a straight line, exposing the bed of the nail, and, proximally, the matrix on that side. By means of a sharp small bone curet, the exposed matrix is completely curetted away. The wound is thoroughly swabbed with a cotton applicator soaked in 95 per cent phenol, and then with alcohol. This is done to destroy any fragment of matrix that may have become implanted in the wound. If considerable infection is present a small wick of iodoform gauze may be inserted under the flaps. No special closure of the wound is necessary. The flaps will fall back into place themselves and any dead space will be eliminated by the application of a tight dressing. The wound is first covered by a layer or two of

petrolatum gauze, snugly encircling the terminal phalanx. A few small pieces of plain gauze are then similarly applied, and several turns of a roller bandage made. The tourniquet is cut, starting considerable fresh bleeding, but this is promptly controlled by completing the bandage. On the day following operation, the patient wears a cut-out shoe and is permitted to walk and resume as much of his normal occupation as he desires. On the second day after operation he returns for his first dressing, at which time the blood encrusted dressings are removed; if a drain has been inserted, it too is removed; a smaller petrolatum gauze dressing is then applied. On the sixth or seventh postoperative day, when healing has well progressed, two or three 2 by 0.5 cm. strips of adhesive tape are applied directly to the wound in such a way as to pull the lateral flap in the direction of the cut edge of the nail. A small dry dressing is applied over this. Thereafter, dressings of adhesive tape are applied every three or four days until complete healing has occurred. Beginning about the eighth day, the patient makes a daily attempt to wear his regular shoe. Twenty-nine operations were performed on twenty patients in accordance with the described technic. All were followed for at least six months, some as long as eighteen months. There was a complete and satisfactory cure in all.

Rectal Evipal as Complete Anesthesia.—Hogan reports observations on 200 patients given rectal evipal as a complete anesthesia. The depth of anesthesia is easily controlled by means of metrazol. Postoperative pulmonary complications have been markedly reduced in his hospital since the introduction of the technic. Postoperative distress has decreased and hospitalization of the patient has been reduced by from one to three days. In some cases the relaxation in the abdomen has not been satisfactory and it is his belief that the addition of a small amount of ether in oil to the rectal evipal will eliminate this factor. Clinical observations along these lines are proceeding.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

21: 593-736 (Nov.) 1937

*Criteria of Cure of Gonococcic Infections in Women. L. R. Wharton, Baltimore.—p. 593.

Treatment of Syphilis with Hyperpyrexia, with Observations on Prognosis of Optic Atrophy. F. R. Menagh, Detroit.—p. 609.

Inability to Cultivate Virus of Lymphogranuloma Venereum on Chick Membrane. R. B. Dienst, E. S. Sanderson and R. B. Greenblatt, Augusta, Ga.—p. 622.

Studies in Cardiovascular Syphilis: IV. Influence of Treatment of Early Syphilis on Incidence of Cardiovascular Syphilis. J. E. Kemp and K. D. Cochems, Chicago.—p. 625.

Administration, Location, Policies, Management, Physical Equipment and Personnel Standards of a Syphilis Clinic. R. S. Dixon, Detroit.—p. 634.

Treatment of Syphilis with Mapharsen. J. W. Marshall, Portland, Ore.—p. 645.

Accidental Transmission of Syphilis by Blood Transfusion. J. V. Klauder, Philadelphia, and T. Butterworth, Reading, Pa.—p. 652.

*Use of Ducrey Vaccine in Diagnosis. Anna Dean Dulaney, Memphis, Tenn.—p. 667.

Toxic Effects of Bismuth, with Especial Reference to Renal Damage: Report of Case of Anuria. A. C. Eitzen, Hillsboro, Kan.—p. 674.

Suggested Specifications for Bismuth Subsalicylate in Oil. W. F. Reindollar, Baltimore.—p. 679.

A Syphilis Nomenclature for Diagnosis Files in Clinics and Hospitals. J. E. Moore and P. Padget, Baltimore.—p. 683.

Cure of Gonococcic Infections in Women.—In order to find a basis for the criteria of cure in gonorrhea Wharton followed up his seventy-six private patients that he treated in the last ten years. There were twenty-one cases in children, thirty-three cases in adult women treated without operation and twenty-two cases also in adult women receiving radical treatment. In gonorrheal vaginitis of children, his criterion of cure is complete absence of gonococci in smears for approximately six consecutive months, the smears being taken at least once a month. Gonococcic vaginitis in children can be completely and permanently cured and it can be determined whether a child has been rendered noninfectious. The first criterion is a long observation of these patients through the various stages and final localization of the disease, and the knowledge that these infected foci have been either excised surgically or destroyed completely by the actual cautery. The other criteria are repeated follow-up examinations with negative observations for one year, repeated negative smears and continuously negative history of infection, both personal and marital. The complement fixation test may eventually deserve to be included among the criteria of cure. There is no single, simple, easy test which will infallibly indicate the presence or absence of gonorrhea. Approximately 90 per cent of the author's patients are well. Some have married and borne healthy children without any infection in either the husband or wife. Therefore gonorrhea in women can be cured and there are reliable criteria of cure.

Use of Ducrey Vaccine in Diagnosis.—Dulaney presents the results of 260 skin tests on 125 individuals, from which it is seen that an easily demonstrated allergy is present in persons infected with Haemophilus ducreyi and that a positive cutaneous reaction is indicative of present or past infection. In fifty patients showing lesions that were clinically chancroid, positive reactions were obtained in forty-six. Two of the negative results were given by patients in the early stages of the disease who had not developed buboes, and it is accepted that such involvement increases cutaneous reactivity. Two patients with typical lesions of the surface and buboes failed to react to either the Ducrey or the Frei antigen. Cutaneous sensitivity is demonstrable early in the disease, as early as ten days (patient's history) after the appearance of the ulcer, but in most cases allergy manifests itself at a later date. The reaction increases in intensity with time. Cutaneous sensitiveness, once developed, is very lasting and must always be remembered in practical use of the test. While both chancroidal pus and bacillary antigens may be used for cutaneous testing purposes, the latter elicits much more definite reactions. It also affords a method of standardizing such a diagnostic procedure. The high incidence of coexisting venereal lymphogranuloma and chancroidal infection necessitates a careful selection of material for antigens and especially for Frei tests.

Archives of Neurology and Psychiatry, Chicago

38: 913-1134 (Nov.) 1937

Sensory Functions of Optic Thalamus of the Monkey (Macacus Rhesus): Symptomatology and Functional Localization Investigated with Method of Local Strychninization. J. G. Dusser de Barenne, New Haven, Conn., and O. Sager, Bucharest, Rumania.—p. 913.

Electrical Stimulation of Cortex Cerebri of Cats: Responses Elicitable in Chronic Experiments Through Implanted Electrodes. S. L. Clark and J. W. Ward, Nashville, Tenn.—p. 927.

*Phenylpyruvic Oligophrenia: Introductory Study of Fifty Cases of Mental Deficiency Associated with Excretion of Phenylpyruvic Acid. G. A. Jervis, Thiells, N. Y.—p. 944.

"Cold Pressor Test" in Tension and Anxiety: Cardiochronographic Study. B. V. White Jr. and E. F. Gildea, New Haven, Conn.—p. 964.

Curve for Sugar Content of Blood Following Encephalography: Comparison with Usual Curve for Dextrose Tolerance. M. Scott, Philadelphia.—p. 985.

Studies in Diseases of Muscle: I. Metabolism of Creatine and Creatinine in Progressive Muscular Dystrophy. A. T. Milhorat and H. G. Wolff, New York.—p. 992.

Encephalomyelitis Complicating Measles. N. Malamud, Ann Arbor, Mich.—p. 1025.

A Form of Chronic Epidemic Encephalitis Simulating the Landouzy-Dejerine Type of Progressive Muscular Dystrophy: Value of Studies on Creatine in Conjunction with Ingestion of Amino Acid as Aid in Differential Diagnosis. S. R. Dean, Taunton, Mass.—p. 1039.

Disturbances of Activity in Case of Schizophrenia. A. Angyal, Worcester, Mass.—p. 1047.

Neuro-Epithelial Cyst of the Third Ventricle: Report of Case with Recovery Following Operation. W. J. Gardner and O. A. Turner, Cleveland.—p. 1055.

Phenylpyruvic Oligophrenia.—Jervis studied fifty cases of phenylpyruvic oligophrenia. Twenty-one patients were inmates at Letchworth Village; thirteen patients were examined at the Wassaic State School, eight at the Rome State School and eight, who were siblings of institutionalized patients, were examined at their respective homes. Examination of the members of the family of thirty-five patients showed that phenylpyruvic acid did not in any instance occur in the urine of mentally normal members. The clinical manifestations, in their constitutional, neurologic and psychologic aspects, appear to occur with a certain constancy and are sufficiently characteristic to afford justification for regarding them as constituting a fairly well defined clinical syndrome. Critical examination of the anamnestic data seems to exclude any relation of exogenous agencies to the etiology of the disease, whereas the family incidence of the disease suggests that a genetic mechanism is of etiologic significance. Statistical elaboration and critical analysis of the genetic figures afford

justification for regarding the condition as determined by a single recessive gene substitution. Clinically, the disease is characterized by pronounced intellectual defect coexisting with neurologic symptoms. These consist of extrapyramidal manifestations (rigid posture, muscular hypertonus and hyperkinesias) and exaggeration of the deep reflexes. Characteristic constitutional features are found in the majority of cases. From a biochemical point of view the condition appears to be an error of the metabolism of phenylalanine, consisting essentially of a failure to oxidize further a normal catabolite, phenylpyruvic acid, which consequently is excreted as such in the urine.

Arch. of Physical Therapy, X-Ray, Radium, Chicago

18: 609-672 (Oct.) 1937

Dosimetry in Short Wave Therapy: Instrument for Dosage Determination of Patient's Circuit. E. Mittelmann, Vienna, Austria.—p. 613.
Research Methods and Physical Therapy. H. A. Carter, Chicago.—p. 619.
Physical Therapy of Chronic Atrophic Arthritis. E. M. Smith, Little Rock, Ark.—p. 622.
*Postural Defects Related to Arthritis. E. F. Hartung, New York.—p. 626.
Chronic Arthritis of the Spine: Its Relation to Rheumatoid Disorders. M. F. Lautman, Hot Springs, Ark.—p. 630.
Proceedings of the First International Congress of Short Wave Therapy in Vienna. H. F. Wolf, New York.—p. 636.
Alternate Suction and Pressure Therapy in Peripheral Obliterative Vascular Diseases. J. R. Veal, New Orleans.—p. 640.
Transcerebrospinal Calcium Iontophoresis in Bronchial Asthma: Preliminary Note. A. Barnett, Brooklyn.—p. 646.

Postural Defects Related to Arthritis.—Hartung declares that defects in bodily posture affect patients with arthritis in five ways. 1. Poor posture is a mechanically inefficient carriage and therefore requires an undue amount of energy in standing and sitting. In this way it adds one more burden to the already overburdened constitutional inadequacy of these patients. 2. It produces ptosis of the gastro-intestinal tract and decreases the vital capacity of the lungs. This embarrasses the normal function of these organs. 3. It predisposes to pains in the lower part of the back. 4. It causes undue trauma at certain joints, predisposing these to the localization of arthritis. In osteo-arthritis, in which the process is generalized, this static trauma localizes the development of pain in certain crucial areas such as in the lumbosacral and cervical spine, the knees and the feet. 5. It has a depressing psychologic effect. Chronic arthritis is a constitutional disease and until a clear idea is had of its etiology the most effective treatment must be directed toward the various constitutional derangements presented by these patients. Muscular exercise in itself unless properly planned will not correct postural defects. The keystone of defective posture is often a lumbar lordosis and the associated pelvic tilt. To correct lumbar lordosis, emphasis is placed not on exercises alone but on developing a conscious control especially of the gluteal and abdominal muscles. Without gaining this neuromuscular control, no amount of exercise will bring about satisfactory improvement in posture.

Connecticut State Medical Society Journal, Hartford

1: 459-558 (Nov.) 1937

Reminiscences in the Development of Gynecology. H. A. Kelly, Baltimore.—p. 459.
Conservative Treatment of Syphilis. A. K. Poole, New Haven—p. 468.
Chemical Transmission of Nerve Impulses and Neuromimetic Drug Action. L. S. Goodman, New Haven.—p. 473.
The Place of Cesarean Section. F. C. Irving, Boston.—p. 483.
Studies in Vitamin C Content of Blood in Patients wth Dental Abnormalities. D. Weisberger, Boston.—p. 492.
Clinical Picture of Suppurative Lesions of Petrosal Pyramid. S. J. Kopetzky, New York.—p. 497.
*Protamine Zinc Insulin: Improvement in Carbohydrate Tolerance: Clinical Observations. B. Greenhouse, New Haven.—p. 503.
The State Program for Crippled Children Under the Social Security Act. A. Steindler, Iowa City.—p. 505.
The Recent Revolution in Anesthesia. H. R. Griffith, Montreal.—p. 509.
Prepaid Hospital Service. C. Barker, New Haven.—p. 515.

Protamine Zinc Insulin and Carbohydrate Tolerance.—Greenhouse attributes the increased carbohydrate tolerance of diabetic patients given protamine zinc insulin to the continuity of its effect and its prolonged action. It furnishes a basic insulin supply by creating a depot from which insulin is regularly and continuously liberated so that the body has available a supply of insulin at all times over a period of at least twenty-four hours. The metabolism of the diabetic patient is thus more adequately stabilized, offering particular respite to the pancreas and liver. Protamine zinc insulin finds its greatest usefulness in the case in which the diabetes is in part at least functional, rather than in cases of diabetes in which the pancreas is so sclerosed as to allow for no improvement. Improvement occurred most frequently in the large middle-aged group of patients.

Journal of Biological Chemistry, Baltimore

121: 1-372 (Oct.) 1937. Partial Index

Relation of Vitamin D to Skin Respiration. A. K. Presnell, Cincinnati.—p. 5.
Abscess Nitrogen Metabolism in Anemic and Nonanemic Dog: Reserve Stores of Protein Apparently Involved. F. S. Daft, Frieda S. Robscheit-Robbins and G. H. Whipple, Rochester, N. Y.—p. 45.
Composition of Tissue Proteins: III. Arginine in Placenta. S. Graff and Ada M. Graff, New York.—p. 79.
Influence of Bile Salts on Enzymatic Synthesis and Hydrolysis of Cholesterol Esters in Blood Serum. W. M. Sperry and V. A. Stoyanoff, New York.—p. 101.
Effect of Prolonged Low Protein Diet on Serum Lipids of Dogs. I. H. Page, L. E. Farr and A. A. Weech, New York.—p. 111.
Studies on Chemistry of Blood Coagulation: IV. Lipid Inhibitors of Blood Clotting Occurring in Mammalian Tissue. E. Chargaff, New York.—p. 175.
Id.: V. Synthetic Cerebroside Sulfuric Acids and Their Action in Blood Clotting. E. Chargaff, New York.—p. 187.
Amount of Iodine in Blood. E. J. Baumann and Nannette Metzger, New York.—p. 231.
Studies on Biologic Oxidations: IX. Oxidation-Reduction Potentials of Blood Hemin and Its Hemochromogens. E. S. G. Barron, Chicago.—p. 285.
Relationship of Blood Cholesterol to Hemoglobin and Serum Protein. H. Schwarz and H. H. Lichtenberg, New York.—p. 315.
Studies on Role of Bromine in Nutrition. P. S. Winnek and A. H. Smith, New Haven, Conn.—p. 345.
Turnover of Phospholipids in Intestinal Mucosa. R. G. Sinclair and C. Smith, Rochester, N. Y.—p. 361.

Journal of Clinical Investigation, New York

16: 833-950 (Nov.) 1937

Bisulfite Binding Power of Blood in Health and in Disease, with Especial Reference to Vitamin B_1 Deficiency. F. H. L. Taylor, S. Weiss and R. W. Wilkins, Boston.—p. 833.
Estimation of Subcutaneous Tissue Pressure by a Direct Method. G. E. Burch and W. A. Sodeman, New Orleans.—p. 845.
Clinical Studies of Blood Volume: III. Changes in Blood Volume, Venous Pressure and Blood Velocity Rate in Chronic Congestive Heart Failure. J. G. Gibson 2d and W. A. Evans Jr., Boston.—p. 851.
Measurement of Glomerular Filtration: Creatinine, Sucrose and Urea Clearances in Subjects Without Renal Disease. A. W. Winkler and J. Parra, New Haven, Conn.—p. 859.
Id.: Creatinine, Sucrose and Urea Clearances in Subjects with Renal Disease. A. W. Winkler and J. Parra, New Haven, Conn.—p. 869.
Convenient Method for Determination of Approximate Cardiac Output in Man. J. S. Donal Jr., Philadelphia.—p. 879.
*Chronic Pyelonephritis and Arterial Hypertension. A. M. Butler, Boston.—p. 889.
Allergy and Desensitization in Tuberculosis. H. S. Willis and C. E. Woodruff, Northville, Mich.—p. 899.
Relation of Serum Calcium to Serum Albumin and Globulins. A. B. Gutman and Ethel Benedict Gutman, New York.—p. 903.
Studies on Serum Proteins: I. Identification of Single Serum Globulin by Immunologic Means: Its Distribution in Serums of Normal Individuals and of Patients with Cirrhosis of Liver and with Chronic Glomerulonephritis. F. E. Kendall, New York.—p. 921.
*Quantitative Study of Oxidation of Glucose in Normal and Diabetic Men. J. M. Sheldon, M. W. Johnston and L. H. Newburgh, Ann Arbor, Mich.—p. 933.

Chronic Pyelonephritis and Arterial Hypertension.—During the last ten years fifteen children between 3 and 11 years of age were observed by Butler at necropsy to have pyelonephritis. Records of the blood pressures of seven of these patients are not available. The records of the blood pressures for the remaining eight patients show systolic pressures ranging from 250 to 140 mm. of mercury and diastolic pressures from 170 to 110 mm. of mercury, the average systolic and diastolic pressures being respectively 190 and 140 mm. of mercury. Two of these patients had hypertensive crises and died of cardiac failure before significant nitrogen retention occurred. The clinical histories of two others of the group studied pathologically indicated that the pyelonephritis and hypertension preceded severe nitrogen retention. During the same ten years three patients with pyelonephritis and hypertension died but permission for necropsy was not obtained. The histories of two of these patients indicate that the pyelonephritis and hypertension preceded significant renal insufficiency and nitrogen retention. During this period nine patients with pyelonephritis and hypertension were admitted to the hospital and when last seen were living. Of these patients only one had renal insufficiency, and in this one the pyelonephritis

and hypertension preceded the appearance of the diminished renal function. Thus there have been fifteen patients (six dead and nine living) who have had chronic pyelonephritis and hypertension over a period of years before there was appreciable diminution in the function of the kidney. There is no definite proof that the pyelonephritis preceded the hypertension. A patient, coincident with a ureteral calculus, was found to have a unilateral pyelonephritis and during the course of the next eight months hypertension and cardiac failure developed. The removal of the one infected kidney was followed by clearing of the urine and a return of the blood pressure to normal, where it has remained for twenty months. There is strong evidence that the pyelonephritis preceded the hypertension and in some way had a causal relation to it. The study has led to the hypothesis that the hypertension might well be related to the local effect of the pyelonephritis rather than to the renal insufficiency encountered late in the disease.

Oxidation of Dextrose in Normal and Diabetic Men.—Sheldon and his collaborators compared the oxidation of dextrose in normal and diabetic men. When the three normal male subjects were studied in the fasting state, the amount of carbohydrate oxidized in the four hour period became larger as the carbohydrate of the preparatory diet was increased. This effect was consistently obtained when the carbohydrate in the preparatory diet was varied between 25 and 500 Gm. Further, when the dextrose was ingested at the beginning of the experimental period in amounts from 50 to 200 Gm., even though the carbohydrate preparation had been the same, the oxidation of dextrose was increased. When both the carbohydrate of the preparatory and chamber periods were simultaneously increased, the oxidation of dextrose was additive. The three diabetic subjects studied were free of any disease other than the diabetes mellitus. The amount of dextrose oxidized in the four hours was dependent on the severity of the patient's disease. However, the response to increasing the dextrose of the chamber period is similar to the response of the normal subjects, but quantitatively reduced. When the same subjects were studied after a period of from twenty-three to thirty-five days of constant hyperglycemia and glycosuria, the amount of dextrose oxidized in four hours stayed at a constant level, even though the dextrose of the chamber period was increased from 0 to 100 Gm. Emphasis is placed on the inability to increase oxidation of dextrose in response to the ingestion of increased amounts of dextrose, a marked contrast to the normal controls, who oxidized more dextrose when they ingested more of it. Increasing the carbohydrate preparation from two to three times above the tolerance of the diabetic patients resulted in but a slight increase in the amount of dextrose oxidized. This slight increase may be attributed to the associated hyperglycemia, which produced a maximal stimulation of the mechanism for the utilization of carbohydrate. Once the maximal stimulation has been reached, further ingestion of dextrose can never result in additional oxidation.

Journal of Experimental Medicine, New York

66: 527-652 (Nov.) 1937

Studies on Experimental Hypertension: VI. Effect of Section of Anterior Spinal Nerve Roots on Experimental Hypertension Due to Renal Ischemia. H. Goldblatt and W. B. Wartman, Cleveland.—p. 527.
*Mode of Action of Sulfanilamide in Experimental Streptococcic Empyema. F. P. Gay and Ada R. Clark, New York.—p. 535.
Studies on Role of the Spleen in Experimental Poliomyelitis. E. H. Lennette, Chicago.—p. 549.
Globin Utilization by Anemic Dog to Form New Hemoglobin. Freda S. Robscheit-Robbins and G. H. Whipple, Rochester, N. Y.—p. 565.
Panmyelophthisis with Hemorrhagic Manifestations in Rats on Nutritional Basis. P. György, H. Goldblatt, F. R. Miller and R. P. Fulton, Cleveland.—p. 579.
Relation of Altered Local Tissue Reactivity (Shwartzman Phenomenon) to Infection and Inflammation. A. R. Moritz, Cleveland.—p. 603.
Bactericidal Action of Human Serum on Hemolytic Streptococci: III. Studies Concerning: (1) Significance of Hydrogen Ion Concentration in Relation to Streptococcidal Action of Serum; (2) Effect of Reducing Agents on Phenomenon. W. S. Tillett and C. C. Stock, Baltimore.—p. 617.
Changes in Blood Vessels (Capillary Fragility) with Inflammation. E. Zander, New York.—p. 637.

Action of Sulfanilamide in Empyema.—Gay and Clark state that sulfanilamide prevents the evolution of an invariably fatal streptococcic empyema in rabbits when it is given repeatedly and in sufficient doses subcutaneously. Complete sterilization of the inoculated cavity occurs on approximately the second day. The serum, defibrinated blood and artificial pleural exudate of similarly treated animals inhibits the growth of the same streptococcus in the test tube, but even repeated doses of such treated blood serum fail to sterilize the culture. The coccic chains grown in such drugged serum are elongated and present pleomorphic and metachromatic organisms and may give rise to colonies that are at first less predominantly mucoid in appearance. Such organisms have lost little if any of their virulence. Cooperation on the part of locally derived clasmatocytes is apparently required in complete sterilization of the animal body. Sulfanilamide apparently produces a bacteriostasis sufficiently marked to protect the accumulated leukocytes and to allow the natural defense macrophages to accumulate. There is direct evidence that the drug does not in itself stimulate the mobilization of the macrophages. There is no evidence that the cell reaction which finally accounts for disposal of the organisms is other than local.

Journal of Pediatrics, St. Louis

11: 455-606 (Oct.) 1937

Substitution of Olive Oil for Butter Fat in Infant Feeding. M. L. Blatt and E. H. Harris, Chicago.—p. 455.
Multiple Facial Anomalies. E. T. McEnery and J. Brennemann, Chicago.—p. 468.
Unusual Congenital Anomaly of the Spine and Ribs: Extensive Spina Bifida Occulta, Probable Included Twin, and an Uncommon Fusion Anomaly of the Ribs. M. Cooperstock and E. R. Elzinga, Marquette, Mich.—p. 475.
Active Scurvy in an Infant Receiving Orange Juice. E. A. Hagmann, Detroit.—p. 480.
Variability of the Kahn Reaction in Children. H. B. Rothbart, Detroit.—p. 484.
*Untreated Seronegative Mothers of Syphilitic Children: Report of Two Cases. J. R. Waugh, Norfolk, Va.—p. 490.
*Fever Therapy in Children. L. Spekter, Hartford. Conn., and A. McBryde, Durham, N. C.—p. 499.
Listerella Meningitis: Report of Additional Case with Necropsy Findings. Mary A. Poston, S. E. Upchurch and Marguerite Booth, Durham, N. C.—p. 515.
Staphylococcus Aureus Meningitis: Report of Case with Recovery. R. L. Jackson, Iowa City.—p. 518.
Antirachitic Efficiency of Irradiated Cholesterol. J. S. Hood, Clearwater, Fla., and Irene Ravitch, Baltimore.—p. 521.
Sudden Death Due to Mercurial Diuretics. H. M. Greenwald and S. Jacobson, Brooklyn.—p. 540.
Acute Naphtha Poisoning: Report of Case in Infant. J. P. Price and F. Harrison, Florence, S. C.—p. 547.
Congenital Bronchogenic Cyst of Mediastinum: Report of Case. J. E. Alford, Buffalo.—p. 550.
Abscess of Epiglottis in an Infant: Case Report. E. L. Noone, Drexel Hill, Pa., and W. P. Shields, Philadelphia.—p. 556.
Thrombocytopenic Purpura Haemorrhagica: Two Cases Treated with Parathyroid Hormone and Calcium Gluconate. M. L. Ainsworth, S. D. Edelman and R. I. Fried, Columbus, Ohio.—p. 559.
Hemorrhage from Meckel's Diverticulum. R. A. Higgons and J. E. Gundy, Port Chester, N. Y.—p. 563.
Technic of Intravenous Transfusion of Blood in New-Born Infants. W. H. Prioleau, Charleston, S. C.—p. 568.

Untreated Seronegative Mothers of Syphilitic Children.—Waugh states that only two untreated seronegative mothers of children with prenatal syphilis were admitted to the United States Public Health Service Venereal Disease Clinic, Hot Springs, Ark., during the seven years 1930 to 1936. Blood serum Wassermann reactions, spinal fluid examinations and careful physical examinations revealed no evidence of syphilis in these two mothers. There is no doubt that their two children had prenatal syphilis rather than acquired syphilis, as both children had bilateral interstitial keratitis, hutchinsonian upper central incisors, saddle noses and 4 plus blood serum Wassermann reactions.

Fever Therapy in Children.—Spekter and McBryde believe that severe reactions of fever therapy can be avoided by careful observation of the patient before and during treatment. The benefits derived from fever therapy outweigh the risks, especially in gonorrheal infections. Treatment at high temperatures is not devoid of danger. At Duke Hospital about 430 fever treatments (at temperatures varying from 104 to 106.7 F.) have been given to 280 patients (thirty-two children, 248 adults). Four deaths occurred in adults. If the patient tolerates the first three hours of fever, the remaining two to nine hours of treatment usually will progress smoothly, provided there is an adequate intake of fluid, the patient is fairly quiet and the temperature is not allowed to go above 106.7 F. In the thirty-

two children, artificial fever has been used in treating gonorrheal infections, chronic infectious arthritis, syphilis, chorea, encephalitis, Hodgkin's disease, tuberculous meningitis, undulant fever, interstitial keratitis and leukemia.

Kentucky Medical Journal, Bowling Green

35: 497-538 (Nov.) 1937

Blindness and Its Prevention. H. G. Reynolds, Paducah.—p. 499.
Subordinate Obligations of the Surgeon. J. A. Ryan, Covington.—p. 505.
A Tribute to My Profession. A. W. Nickell, Louisville.—p. 508.
Importance of Early Diagnosis and Treatment of Acute Inflammation of Middle Ear. G. F. Doyle, Winchester.—p. 517.
Complete Inversion of Uterus: Report of Case Successfully Treated by Manual Reposition. J. D. Hancock, Louisville.—p. 520.
The Common Cold. A. A. Shaper, Louisville.—p. 523.
Some Traditions and Responsibilities of the Medical Profession. E. L. Bishop, Knoxville, Tenn.—p. 526.
Clinical Application of Sedimentation Rate, or Suspension Stability. R. R. Elmore, Louisville.—p. 530.
Treatment of Pulmonary Tuberculosis in a Rural Community, with Particular Reference to Bilateral Disease. O. A. Beatty, Glasgow.—p. 533.

Missouri State Medical Assn. Journal, St. Louis

34: 403-430 (Nov.) 1937

The Opportunities of Internship. J. Basman, St. Louis.—p. 403.
Advantages of Service in a State Hospital for Mental Diseases. E. F. Hoctor, Farmington.—p. 404.
Advantages of Service in the State Sanatorium. R. H. Runde, Mount Vernon.—p. 406.
The Psychologic Approach to the Handicapped Child. W. J. Stewart, Columbia.—p. 408.
*The Acute Alcoholic. W. F. Friedewald, St. Louis.—p. 410.
Modern Methods of Typing the Pneumococcus. R. O. Muether, St. Louis.—p. 412.
Simultaneous Malignant Change in Benign Tumors. W. E. B. Hall, St. Joseph.—p. 415.
A Simple Continuous Suction Device with Some New Indications and Uses. M. Goldenberg and I. C. Middleman, St. Louis.—p. 416.

The Patient with Acute Alcoholism.—Friedewald states that during the last two years there were 1,887 cases of alcoholism admitted to the St. Louis City Hospital. About two thirds of the cases were classified as acute. Fifty of the patients died and necropsies were obtained on nine of them. In these cases alcohol was considered either the immediate or the contributory cause of death. In the necropsies all but two cases showed marked fatty infiltration of the liver. The brain was examined in only three of the cases; two showed cerebral edema and the other showed rather marked cerebral atrophy. Four cases showed a bronchopneumonia. One patient, a man aged 45, a chronic alcohol addict who entered the hospital vomiting blood and in shock, at necropsy showed an acute gastritis with erosion of blood vessels and resultant hemorrhage. While the patient with acute alcoholism can usually be given a good prognosis for recovery, a number of these cases are real medical emergencies and require accurate diagnosis and active treatment. The treatment depends on the condition of the patient and the stage of the alcoholism. Ordinarily evacuation of the stomach by means of a stomach tube followed by a saline purgative is indicated. Apomorphine may be used, which also acts as a hypnotic. In the excitement stage, sedatives are necessary. Paraldehyde, bromides and chloral hydrate are the drugs used most commonly. In the depressant stage caffeine or strychnine is used as a stimulant. Acute alcoholic coma causes a dangerous respiratory depression, paralysis and cyanosis. Death may be prevented and recovery accelerated by the inhalation of 90 per cent oxygen and 10 per cent carbon dioxide for a time sufficient to reestablish normal color and respiration. Since the alcoholic patient is usually in a state of starvation and avitaminosis, he must be given a high caloric diet rich in all vitamins, supplemented with large doses of vitamin B. Patients showing cerebral edema with symptoms of increased intracranial pressure are given chloral hydrate and sodium bromide rectally for sedation. Saline purgatives and hypertonic dextrose intravenously aid in relieving the cerebral edema. Repeated spinal drainage also is recommended. A complication that can be overlooked easily is that of hypoglycemia. Most chronic alcohol addicts have fatty livers and there is little glycogen present. Fractures of the skull, lacerations, bruises, and the like must always be kept in mind when examining an acute alcoholic patient. Fracture of the skull can be easily overlooked in an unconscious alcoholic patient.

Nebraska State Medical Journal, Lincoln

22: 405-444 (Nov.) 1937

Surgical Treatment of Primary Carcinoma of the Lung. R. H. Overholt, Boston.—p. 405.
Early Prognosis in Pneumococcic Pneumonia. W. W. Waddell, Beatrice.—p. 412.
Removable Internal Fixation After Reduction of Certain Fractures, by the Use of Beaded Wire. J. E. M. Thomson and C. F. Ferciot, Lincoln.—p. 415.
A New Era in Anesthesia. J. Weinberg, Omaha.—p. 418.
Cyclopropane Anesthesia from the Standpoint of the Surgeon. J. W. Duncan, Omaha.—p. 421.
Cyclopropane Anesthesia from the Standpoint of an Anesthetist. B. H. Harms, Omaha.—p. 425.
Persistent Enlarged Thymus Gland: Case Report. J. C. Eagan, Madison.—p. 429.

New England Journal of Medicine, Boston

217: 687-724 (Oct. 28) 1937

Epidemiologic and Immunologic Experiments on Rabies. L. T. Webster, New York.—p. 687.
The Dietetic Treatment of "Eczema" in Early Infancy. L. W. Hill, Boston.—p. 690.
Maternal Mortality at the Boston Lying-In Hospital in 1933, 1934 and 1935. F. C. Irving, Boston.—p. 693.
*Narcolepsy and Its Treatment with Benzedrine Sulfate. H. Ulrich, Boston.—p. 696.
Cardiospasm: Methods of Procedure in Presence of Serious Esophagitis: Report of Two Cases. N. Canfield, New Haven, Conn.—p. 702.

Narcolepsy and Its Treatment with Benzedrine Sulfate.—Ulrich reexamined his cases of narcolepsy that have been treated with benzedrine sulfate for nearly two years. No permanent deleterious effects were noted, and there was no evidence of habit formation. Some of the patients complained of temporary disturbances, including anorexia, especially if the drug was taken before meals. Slight temporary elevation of the blood pressure and of the basal metabolic rate was produced in a few cases, but no permanent effect of that nature was observed. Although the need for caution in the presence of vascular hypertension is emphasized, a case is reported in order to show that hypertension, arteriosclerosis and senility are not absolute contraindications to the use of benzedrine in suitable cases. Loss of weight was the result of the treatment in several obese patients. This is believed to have been due in part to the lessened appetite that may result from the use of the drug and in part to the change from periodic quiescence to a state of greater mental and physical activity. Harm may come from the careless and uncontrolled use of benzedrine in the treatment of narcolepsy especially in otherwise healthy young persons. Dibenzyl carbinamine, a related compound, was tried in a few cases. It had no beneficial action on the narcoleptic state, and its deleterious effect on the gastro-intestinal tract was greater than that of benzedrine. Oral medication with benzedrine sulfate appears to be the only satisfactory method of treatment.

New Orleans Medical and Surgical Journal

90: 245-314 (Nov.) 1937

Diabetes: Experiences with Protamine Insulin. I. I. Lemann, New Orleans.—p. 245.
The Principles of Surgery on Diabetic Patients. U. Maes, New Orleans.—p. 249.
Diabetes in Childhood. C. J. Bloom, New Orleans.—p. 252.
The Pathology of Diabetes Mellitus. S. Warren, Boston.—p. 260.
Some Minor Disorders of the Female Urethra. E. B. Vickery, New Orleans.—p. 262.
Treatment of Bronchial Asthma: Report of 244 Follow-Up Cases. W. H. Browning, Shreveport, La.—p. 269.
*Infections of the Middle Ear. J. T. Crebbin, Shreveport, La.—p. 274.
Role of the Orthopedic Surgeon in Treatment of Arthritis. R. B. Osgood, Boston.—p. 279.
Nineteenth Century Contributions to Treatment of Pulmonary Tuberculosis. S. Jacobs, New Orleans.—p. 286.

Infections of the Middle Ear.—Crebbin states that a study of middle ear infections is facilitated by knowledge of the anatomy of the temporal bone, which at birth, and for months thereafter, consists of three distinct parts: the squamozygomatic, the tympanic and the petromastoid. At this period in life these principal parts are held together by a connective tissue which ossifies slowly and, as a rule, the connection between them is imperfect at the end of the first year. Usually there is no sharp demarcation between an infection of the middle ear and infection of the mastoid. The borderline between an attack of acute catarrhal otitis and an attack of acute suppurative otitis is indefinite. The deciding factor

depends on the type and virulence of the invading organism, the resistance of the patient and the anatomic peculiarities. Earache is the most common symptom in acute infections of the middle ear. There is usually tenderness over the mastoid antrum and tip. Deafness may be present. There is loss of appetite and sleep. Temperature is variable and is not a dependable sign. Convulsions and meningitis may be present from the onset. The appearance of the tympanic membrane is characteristic, but this changes with the progress of infection. There is a lack of luster to the membrane and loss of light reflex. There is usually more or less bulging and redness. At times the appearance of the membrane may be gray instead of red. A patient showing these symptoms should have a myringotomy as soon as possible. An early myringotomy performed amid strict surgical surroundings is generally accepted as a safe procedure. A myringotomy will not cure all patients, for further treatment is ordinarily necessary, and even a mastoidectomy may finally be indicated. A liquid diet, with an abundance of fruit juices, and sunshine are indicated. Carotene in oil and cod liver oil preparations are of great help. A hematologic study and repeated roentgenograms should be made in each case. A swab of the pus is taken after a myringotomy or from the cavity after a mastoidectomy and a vaccine prepared and used if there is delay in the cessation of the aural discharge or delay in the healing of the wound. Vaccines are more effective if autogenous, freshly prepared and started in small doses. The author urges that the dry method of treating be followed in all cases of acute suppurative otitis media. An adenectomy and tonsillectomy should be done as soon as the acute symptoms have passed. A thorough conservative treatment is always indicated in an acute suppurative otitis media. If there is no improvement after a reasonable time, a mastoidectomy is indicated. A preliminary transfusion is indicated, especially if the patient is a very sick child or in a weakened condition. Following a mastoidectomy, transfusions will shorten the duration of the disease and hasten the recovery of the patient. Any patient with chronic suppuration of the middle ear is potentially in danger of his life. Infants and young children should be given a general anesthetic, whereas young adults and adults should have a local anesthetic. The author has had most satisfactory results in using the Miller zinc ionization machine in cases that do not respond to the usual accepted treatment in chronic suppurative otitis. Three cases are cited which show the value of this treatment.

Ohio State Medical Journal, Columbus

33: 1189-1292 (Nov.) 1937

Appendicitis: Surgical Care Based on the Pathologic Conditions Present. J. L. DeCourcy, Cincinnati.—p. 1205.
Conduct and Personality Disorders in Certain Types of Pituitary Dyscrasias. H. C. Schumacher, Cleveland.—p. 1209.
Herpes Zoster Ophthalmicus. D. J. Lyle, Cincinnati.—p. 1213.
Meningitis of Otitic Origin. E. P. Shepard, Columbus.—p. 1218.
Pregnancy Complicated by Mitral Stenosis and Toxemia. S. J. Webster and J. E. Morgan, Cleveland.—p. 1225.
Torsion of the Spermatic Cord: Presentation of Case and Short Résumé of the Literature. E. A. Ockuly and F. M. Douglass, Toledo.—p. 1227.
Observations on Use of Benzedrine in Psychoses. Dorothy E. Donley, Amityville, N. Y.—p. 1229.
*Value of Knee-Chest Exercises in Postpartum Retrodisplacement. E. Eichner, Cleveland.—p. 1233.
Rat Bite Fever. J. A. Garvin, Cleveland.—p. 1235.
Vaginal Discharge. A. Cline, Dayton, Ohio.—p. 1236.

Knee-Chest Exercises in Postpartum Retrodisplacement.—Eichner studied 316 women having 402 deliveries in the obstetric service at Mount Sinai Hospital; 22.7 per cent of the uteri of 211 patients instructed in knee-chest exercises during their stay at the hospital were found in a posterior position at their first dispensary examination, while 27.7 per cent of the uteri of the 191 patients not so instructed were retroplaced at their first postpartum examination. In the entire series 101 patients, or 25.1 per cent of the total, had retrodisplacements at their initial postpartum visit. The percentage of posterior displacements increased with the parity from 20 in the primiparas to 41.2 in the quintigravidas; 30.4 per cent of the posterior displacements treated by knee-chest exercises were failures and, of these, six patients responded to the use of a pessary and seven were discharged. In cases in which the pessary failed, the knee-chest position also failed. In twelve patients the uterus became anterior without treatment for the retrodisplacement in an interval less than that required for either pessaries or knee-chest exercises. The conclusion is that knee-chest exercises are valueless in the treatment of postpartum retrodisplacement except during the third and fourth weeks of the puerperium, when these exercises appear to reduce the percentage of displacements.

Physiological Reviews, Baltimore

17: 485-646 (Oct.) 1937

Transmission at Nerve Endings by Acetylcholine. G. L. Brown, London, England.—p. 485.
Transmission of Sympathetic Nerve Impulses. A. Rosenblueth, Boston.—p. 514.
Synaptic and Neuromuscular Transmission. J. C. Eccles, Oxford, England.—p. 538.
Cellular Changes in Anterior Hypophysis, with Especial Reference to Its Secretory Activities. Aura E. Severinghaus, New York.—p. 556.
Cellular Differentiation and Tissue Culture. W. Bloom, Chicago.—p. 589.
Action of Morphine on Digestive Tract. H. Krueger, Ann Arbor, Mich.—p. 618.

Public Health Reports, Washington, D. C.

52: 1519-1562 (Oct. 29) 1937

Sickness Among Male Industrial Employees During the Second Quarter and First Half of 1937. D. K. Brundage.—p. 1523.
The Association of Scurvy with Oral Diseases. F. C. Cady.—p. 1526.
Kentucky's Plan for Public Health Education. A. T. McCormack and Reba F. Harris.—p. 1530.

Southern Medical Journal, Birmingham, Ala.

30: 1043-1144 (Nov.) 1937

Primary Liver Carcinoma: Relation to Yellow Atrophy Cirrhosis. K. M. Lynch, Charleston, S. C.—p. 1043.
Primary Carcinoma of the Ileum. J. W. Nixon, San Antonio, Texas.—p. 1049.
Regional Ileitis with Involvement of Cecum. D. J. Pessagno, Baltimore.—p. 1052.
Congenital Dextrocardia: Report of Ten Cases. L. K. Emenhiser, Oklahoma City.—p. 1055.
Syphilis of the Stomach: Case Report. J. O. Finney, Gadsden, Ala.—p. 1058.
Diagnostic Difficulties in Perinephric Abscess: Case Report. J. R. Stites and J. A. Bowen, Louisville, Ky.—p. 1062.
Pancreatic Lithiasis. J. Witherspoon, Nashville, Tenn.—p. 1064.
*Acute and Chronic Pancreatitis: Clinical Observations. J. Friedenwald, Baltimore.—p. 1067.
Diagnostic Value of Episcleritis. A. G. Wilde, Jackson, Miss.—p. 1074.
Chronic Sinusitis: Complete Operation, Technic and Results in 200 Consecutive Cases. W. R. McKenzie, Baltimore.—p. 1077.
Results of Pyretotherapy at the Vanderbilt University Hospital. R. H. Williams, Nashville, Tenn.—p. 1080.
Study of Mortality Rate and Complications Following Therapeutic Malaria. T. C. C. Fong, Washington, D. C.—p. 1084.
The Present Status in Treatment of Chronic Prostatitis. F. L. Van Alstine, Jackson, Miss.—p. 1089.
The Infant Hygiene Program and Results in Rutherford County, Tennessee. J. B. Black, Murfreesboro, Tenn.—p. 1091.
Pyogenic Psoas Abscesses. F. A. Hoshall, Charleston, S. C.—p. 1097.
Alternating Scoliosis with Proved Etiology: Case. R. A. Milliken, Little Rock, Ark.—p. 1099.

Pancreatitis.—Friedenwald declares that the incidence of acute and chronic pancreatitis is far greater than is recognized and, as the symptomatology of these conditions is usually indefinite, the correct diagnosis is too rarely made. Acute hemorrhagic pancreatitis is ushered in by a sudden violent pain in the epigastrium, with signs of shock, which may suggest rupture of a peptic ulcer, of the gallbladder or even of the appendix. It may be followed by death within a few hours or days. The acute gangrenous form follows the hemorrhagic type, in which the symptoms have been of a milder or subacute form. This condition manifests itself by the appearance of chills, fever and the formation of a mass in the epigastrium within a week or two after the onset of the hemorrhagic stage. The acute suppurative type frequently ensues as a subsequent stage after either of the first two types. It is associated with chills, fever and frequently jaundice, nausea, vomiting and severe epigastric pain. Fat necrosis is an important diagnostic accompaniment, especially of hemorrhagic and gangrenous pancreatitis. When the disease has progressed to the gangrenous and suppurative stages, speedy operation is indicated. Although the symptoms of chronic pancreatitis are rarely definite, its presence should be suspected if in a patient who has suffered from chronic dyspepsia there is present a severe or slight epigastric pain associated with nausea, vomiting, emaciation, extreme weakness, slight jaundice and, occasionally, ptyalism and intermittent glycosuria. In many instances the bulky, soft, fetid and oily stools containing undigested fat and protein aid in arriving at

the diagnosis. The duodenal contents for pancreatic ferments may be markedly diminished in their activity in this condition. In the prophylactic treatment, attention must be especially directed to the early removal of gallstones before complications have occurred and, as preventive measures, a carefully regulated diet should be followed, together with nonsurgical biliary drainages. When the disease is definitely established, immediate operation is advised. If gallstones or pancreatic stones are present, they should be removed and infection overcome.

Surgery, Gynecology and Obstetrics, Chicago

65: 593-720 (Nov.) 1937

Congenital Umbilical Hernia. J. Jarcho, New York.—p. 593.
*Initiation of Respiration in Asphyxia Neonatorum: Clinical and Experimental Study Incorporating Fetal Blood Analyses. R. A. Wilson, M. A. Torrey and Katherine S. Johnson, New York.—p. 601.
Peritoneoscopy. J. C. Ruddock, Los Angeles.—p. 623.
Hemorrhagic or Traumatic Cysts of Mandible. R. H. Ivy and L. Curtis, Philadelphia.—p. 640.
Pituitary Basophilism: Review of Forty-Two Verified Cases, with Report of Personal Case. P. B. Bland and L. Goldstein, Philadelphia.—p. 644.
Roentgen Therapy in Epitheliomas of Maxillary Sinus. J. A. del Regato, Paris, France.—p. 657.
*Cystic Changes in Endometrium. L. M. Randall and W. E. Herrell, Rochester, Minn.—p. 666.
Pathogenesis of Anal Fissure and Implications as to Treatment. P. C. Blaisdell, Pasadena, Calif.—p. 672.
The "Tunnel" Method for Correction of Uterine Retroversion. J. L. Cameron, London, England.—p. 679.
Resection of Head of Pancreas and Duodenum for Carcinoma: Pancreatoduodenectomy. A. Brunschwig, Chicago.—p. 681.
Treatment of Acute Empyema. J. M. Beardsley, Providence, R. I.—p. 685.
Simplified Procedure for Thyroid Exposure. C. G. Heyd, New York.—p. 688.
Bumper and Fender Fractures. F. G. Dyas and M. L. Goren, Chicago.—p. 690.
Fragmentation and Expulsion of a Common Duct Stone into Duodenum by Using Ether and Amyl Nitrite. W. Walters and H. R. Wesson, Rochester, Minn.—p. 695.
Localization and Removal of Foreign (Metallic) Bodies. D. A. Willis, Chicago.—p. 698.
New Suture for Tendon and Fascia Repair. C. M. Gratz, New York.—p. 700.
Operative Cholangiography. P. L. Mirizzi, Córdoba, Argentina.—p. 702.

Initiation of Respiration in Asphyxia Neonatorum.—Wilson and his associates aver that the treatment of asphyxia neonatorum has not kept pace with other advances in obstetrics. A thorough understanding of drugs, anesthetics and resuscitation should be part of the knowledge of every obstetrician. Less than 5 per cent of the volume of oxygen in the blood of the umbilical vein is accompanied by clinical evidence of asphyxia. A brief fall below 1 per cent of its volume is not necessarily fatal, but longer exposures cause permanent damage to the delicate nerve cells of the center and resuscitation is no longer possible. New evidence is presented indicating that the atelectatic lung cannot be opened by gases under pressure in the trachea. Pressures as high as 18 mm. of mercury fail to open alveoli and result in damage to the lung tissue. Lower, and therefore safer, pressures are even less efficacious. Respiratory depressant drugs and anesthetics are discussed and listed in the order of their safety. Morphine alone or in combination has other purposes during labor besides the relief of pain. Because of this it should be administered expertly not less than two hours before delivery. No one method of resuscitation is entirely satisfactory. A method for obtaining graphs of the apnea and early respirations of the new-born is described. The method furnishes conclusive evidence of respiratory status at birth and the effects on the baby of drugs and anesthetics administered to the mother before delivery and shows the efficacy of various methods of resuscitation. In severe cases of asphyxia and respiratory depression, the injection of a respiratory stimulant is logical and to a large extent the only possible way of producing a respiratory gasp. An improved technic for the administration of respiratory and cardiac stimulants, saline solutions and so on by means of the umbilical vein is described.

Cystic Changes in Endometrium.—By microscopic examination of twenty-eight specimens of endometrium Randall and Herrell observed that cystic changes occurred in all phases of the menstrual cycle. In those endometriums in which cystic changes occur in the proliferative phase there is often an accompanying proliferation, so-called hyperplasia, of a greater degree than occurs normally. Thus a polypoid endometrium is usually increased in thickness, although the microscopic picture of the proliferation remains the same. As the differential phase appears and increases, this proliferation is less and less noticeable, but the cystic changes persist. Atypical bleeding was not present in any case in which a well differentiated endometrium was associated with cystic changes. Those tissues in which cystic changes were found in the early differential phase were not infrequently associated with atypical uterine bleeding. In cases in which a cystic endometrium was in the late proliferative phase of the menstrual cycle, atypical bleeding was more frequently present. The essential difference in these specimens of the endometrium is the degree of differentiation which must exist because of a difference in the activity of the hormone of the corpus luteum. There is microscopic evidence that the function of the corpus luteum is not on an all or none basis. Cystic changes are common in the endometriums of women at the beginning of the menopause, when the first phase of ovarian failure is commencing. Ovarian failure is essentially the same among younger women and should be accompanied by the same microscopic appearance of the endometrium.

United States Naval Med. Bulletin, Washington, D. C.

35: 373-560 (Oct.) 1937

Quantitative Study of Mental and Neuromuscular Reactions as Influenced by Increased Air Pressure. C. W. Shilling and W. W. Willgrube.—p. 373.
*Relation of Carbon Dioxide to Artificial Respiration. F. S. Johnson.—p. 380.
Endocrines: Present Day Concepts of Endocrinology. P. F. Dickens and O. J. Brown.—p. 387.
Treatment of Malaria with Atabrine Followed by Plasmochin. C. R. Ball.—p. 418.
Consideration of Mechanism and Treatment of Surgical Shock. T. R. Austin.—p. 426.
To What Extent Is Reality Adjustment Concerned in Selection of Flying Trainee? J. W. Vann.—p. 434.
Copper Sulfate Treatment of Trichophytosis. J. B. Moloney.—p. 440.
Oral Diagnosis as Procedure in Indexing General Diseases Manifested in the Mouth. C. W. Schantz.—p. 441.
Hepatitis, Acute. J. Love.—p. 446.
Study of Syphilis in the Navy. D. T. Prehn.—p. 450.
Evaluation of Recent Trends in Medical Treatment of Peptic Ulcer. E. Ricen.—p. 460.

Relation of Carbon Dioxide to Artificial Respiration.—Johnson points out that a modification (raising and lowering the arms at the elbows alternately with prone pressure) of the Schafer prone pressure method has been proposed by Hederer. An evaluation of this method has indicated the possibility of increasing the pulmonary ventilation in the Schafer method by more than 40 per cent. The great sensitivity of the respiratory center to carbon dioxide is well attested by the fact that artificial respiration applied to the extent of lowering the alveolar carbon dioxide as little as 0.2 per cent below normal is sufficient to cause apnea. On the other hand, when the alveolar carbon dioxide pressure is raised by only 2 mm. the breathing is increased about threefold. If the carbon dioxide of inspired air is increased to 4.5 per cent it is impossible to produce an apneic pause, however forcefully the artificial respiration may be carried out. There seems no reason to avoid the conclusion that every form of manually applied artificial respiration should be accompanied by the inhalation of carbon dioxide whenever possible. The use of an apparatus of the type of the H-H inhalator is recommended in connection with artificial respiration.

Wisconsin Medical Journal, Madison

36: 797-880 (Oct.) 1937

The Blood Sedimentation Rate. M. G. Peterman, Milwaukee.—p. 815.
Measles: Use of Convalescent Serum in Prevention, Modification and Treatment. M. Hardgrove, A. B. Schwartz and Louise F. King, Milwaukee.—p. 817.
Extroversion of Urinary Bladder: Report of Case. W. M. Kearns, Milwaukee.—p. 820.
Transurethral Prostatic Resection for Bladder Neck Obstruction. A. H. Gundersen, La Crosse.—p. 824.
Tuberculosis: The Clinical Phase. H. M. Coon, Statesan.—p. 829.

36: 881-964 (Nov.) 1937

Prevention of Disability: Prevention Through Periodic Observation. M. G. Peterman, Milwaukee.—p. 895.
The Early Diagnosis and Medical Treatment of Poliomyelitis. H. K. Tenney, Madison.—p. 900.
The Prevention of Disability in Poliomyelitis. H. L. Greene, Madison.—p. 903.
Rheumatic Heart Disease in Childhood. H. E. Marsh, Madison.—p. 906.
Acute Osteomyelitis in Children. W. P. Blount, Milwaukee.—p. 910.
Fractures of the Elbow in Children. I. Schulz, Milwaukee.—p. 913.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Archives of Disease in Childhood, London

12: 267-338 (Oct.) 1937

Tumors of Sympathetic Nervous System in Children: Study of Twenty-Five Cases. Ruby O. Stern and G. H. Newns.—p. 267.
Cerebral Tumors in Children: Pathologic Report. Ruby O. Stern.—p. 291.
Studies on Retention of Iron in Childhood. J. H. Hutchison.—p. 305.
*Demonstration of Tubercle Bacillus in Pulmonary Tuberculosis of Childhood. S. Campbell.—p. 321.

Demonstration of Tubercle Bacillus.—Campbell describes the advantages of the various methods of demonstrating the tubercle bacillus and attempts to establish the comparative value of the aids to diagnosis in a series of fifty suspected children. In the efforts to demonstrate the tubercle bacillus in pulmonary tuberculosis, the greatest success was obtained by culture of the washings of the stomach. Of the twelve cases in which the tubercle bacillus was eventually isolated, culture on Loewenstein-Jensen medium was carried out in ten instances and was positive in eight; i. e., 80 per cent. Of the twelve positive washings from the stomach, sputum was obtained in eight instances and of these five, or 63 per cent, disclosed the presence of the bacillus. In addition to the lower proportion of positive results from examination of the sputum the difficulty, indeed the impossibility, of always obtaining the sputum must be taken into consideration. Although the children resent lavage of the stomach, the swallowed sputum can always be obtained. Direct smear of the washings of the stomach was much less frequently positive than was culture. In the ten positive cases in which culture was carried out the organism was found by direct smear in five. Animal inoculation was also less frequently positive, as in only five of the ten cases was the organism isolated. The risk of the animals dying from intermittent disease and the long time required for the test are further drawbacks.

Brain, London

60: 281-376 (Sept.) 1937

Vasomotor Responses in Toes: Effect of Lesions of Cauda Equina. J. Doupe, J. S. M. Robertson and E. A. Carmichael.—p. 281.
*Dural Sinus Thrombosis in Early Life: Recovery from Acute Thrombosis of Superior Longitudinal Sinus and Its Relation to Certain Acquired Cerebral Lesions in Childhood. O. T. Bailey and G. M. Hass.—p. 293.
Abnormalities in Amount and Circulation of Cerebrospinal Fluid Associated with Otitis Media. A. A. McConnell.—p. 315.
Syndrome of Superior Cerebellar Peduncle in the Monkey. A. E. Walker and E. H. Botterell.—p. 329.
Ataxia and Astereognosis of Bulbar Origin. M. David and H. Askenasy.—p. 354.
*Cerebral Infection with Schistosoma Japonicum. J. G. Greenfield and B. Pritchard.—p. 361.

Dural Sinus Thrombosis in Early Life.—Bailey and Hass made a study of three children who presented organized and canalized thrombi in the superior longitudinal sinus. These three instances were found at necropsy in a series of eighty cases of sinus thrombosis of all types. One patient developed acute neurologic disturbances in the course of cardiac decompensation resulting from mitral stenosis of rheumatic origin. At necropsy, organized and canalized thrombi were found in the superior longitudinal and right lateral sinuses. There was a zone of organizing hemorrhage and softening in the cerebral cortex. The other two patients were infants who developed normally up to the time of their acute illnesses, characterized by severe diarrhea and vomiting. During the illness of one patient and shortly after the subsidence of acute symptoms in the other patient, it became obvious that there was impairment of mental function. Death occurred several months later. Portions of the superior longitudinal sinus of each patient contained organized and canalized thrombi. The pathologic changes in the brain and meninges, allowing for such repair as might be expected after a few months, conformed with those changes which are commonly associated with thrombosis of the superior longitudinal sinus of short duration. The authors believe that the study gives support to their contention that certain acquired cerebral defects are due to thrombosis of the superior longitudinal sinus and its sequels. The organized thrombi may be small and easily overlooked, as unless the entire lumen is occluded the process of organization tends to reduce their size greatly. A thorough search of the dural venous sinuses for the presence of organized thrombi may elucidate the causation of some instances of focal cerebral gliosis, "encephalitis" of childhood and spontaneous subdural or subarachnoid hemorrhage.

Cerebral Infection with Schistosoma Japonicum.—Greenfield and Pritchard present clinical and pathologic data which refer to two patients, each of whom presented a symptom complex suggesting the presence of a cerebral tumor and in whom operation disclosed a mass in the brain identified as a collection of eggs of Schistosoma japonicum. If a patient who is known to have sojourned in a part of the world infested with Schistosoma japonicum later has focal epileptic attacks, the possibility should be considered that these may be due to a collection of the eggs of this parasite in the brain. Changes that give support to such a conclusion are undernourishment with a mild secondary anemia and a high eosinophil count in the blood and with a high protein and cellular content in the cerebrospinal fluid. Confirmatory evidence should be looked for in the stools. Eggs of the parasite were found in the stools of both patients. The prognosis is good when operative removal of the tumor is followed by a course of antimony tartrate.

British Journal of Ophthalmology, London

21: 529-576 (Oct.) 1937

Conjunctival Pemphigus. M. H. Whiting.—p. 529.
Some Cases of Paralytic Squint. P. G. Doyne.—p. 531.
Bilateral Mesial Superficial Deficiency of the Sclera. B. Graves.—p. 534.
Divergent Strabismus. E. E. Cass.—p. 538.
Extra-Ocular Influence in Glaucoma (Constitutional Factors). F. Massoud.—p. 559.

21: 577-624 (Nov.) 1937

Dialyzation of Intra-Ocular Fluids. S. Duke-Elder.—p. 577.
*Retinitis of Pregnancy. J. N. Duggan and V. K. Chitnis.—p. 585.
Recognition of Flashing Colored Lights by Persons with Normal and Defective Color Vision. H. V. Corbett and H. E. Roaf.—p. 592.
Norwegian Contribution to Diagnosis and Treatment of Glaucoma. S. Hagen.—p. 597.
Retrobulbar Neuritis in Cases of Serous Meningitis. Elena Puscariu.—p. 599.
The Eye Hospital at Shikarpur, India. R. Buxton.—p. 605.

Retinitis of Pregnancy.—Duggan and Chitnis present three cases of retinitis of pregnancy: the first case represents the characteristic form of retinitis, the second case belongs to the group of toxemia of pregnancy complicated by chronic nephritis and the third one exhibits features resembling the first one, yet its nature remains obscure. There is only one type of retinitis which can be called retinitis of pregnancy, that described by Semple, characterized by sudden onset, edema of retinal tissues, equally sudden cessation on removal of the cause and complete restoration of vision. Whenever chronic nephritis complicates pregnancy, the visual disturbances are due to renal retinitis. This retinitis is associated with high blood pressure, which, together with the signs of retinitis, has a tendency to persist after delivery. This form of retinitis is a useful guide in differentiating chronic nephritis complicating pregnancy from preeclamptic toxemia. It should really belong to the group of cases in which hypertension and chronic nephritis are present before pregnancy. Apart from their differentiating value, lesions of the retina help in estimating the damage done to the vascular tree. In the presence of commencing retinitis, the ophthalmologist should not hesitate to advise interruption of pregnancy.

British Medical Journal, London

2: 783-836 (Oct. 23) 1937

Observation and Experiment and Physiology of the Stomach. A. Hurst.—p. 783.
Abscess of Lung. L. S. T. Burrell.—p. 789.
*Rapid Method for Isolation of Organic Poisons: Preliminary Note. C. P. Stewart, S. K. Chatterji and S. Smith.—p. 790.
Affections of the Eye with Relation to Skin Diseases. J. H. Doggart.—p. 792.
Dermatologic Aspect of Affections of the Eye. G. B. Dowling.—p. 794.
Haemophilus Influenzae Meningitis. H. W. E. Jones.—p. 797.

Rapid Method for Isolation of Organic Poisons.—Stewart and his co-workers find that in the extraction of alkaloidal poisons from the viscera the laborious and time-consuming Stas-Otto process may be replaced by treatment of the minced

material with trichloroacetic acid. This at once yields a water-clear filtrate free from protein and fat, and containing the whole of the alkaloid originally present. From this filtrate the alkaloid can be removed by adsorption on kaolin, from which after neutralization it is eluted by hot chloroform. After removal of the alkaloids, barbital can be adsorbed on charcoal and eluted with ether. The method is being tested further and extended to other organic poisons.

Clinical Journal, London

66: 439-482 (Nov.) 1937

Diagnosis of Ectopic Gestation. W. F. T. Haultain.—p. 439.
Abdominal Pain in Childhood. W. Sheldon.—p. 442.
Preoperative and Postoperative Irradiation in Malignant Disease. W. S. Handley.—p. 449.
Retention of Urine. K. H. Watkins.—p. 452.
Pharyngeal Diverticula. P. J. Moir.—p. 456.
Diagnosis of Scarlatina Group. G. W. Ronaldson.—p. 461.
*Clinical Aspects of Tuberculous Cervical Lymphadenitis. B. C. Thompson.—p. 466.

Clinical Aspects of Tuberculous Lymphadenitis.—Thompson maintains that tuberculosis of the peripheral lymph nodes has decreased considerably during the past quarter of a century, possibly more than any other form of tuberculosis. Nevertheless, it still remains a relatively common disease and in Great Britain is by far the commonest cause of chronic massive enlargement of the lymph nodes. Any large persistent swelling of the lymph nodes of the neck without an obvious local focus is to be regarded as tuberculous until proved otherwise. In 324 cases of peripheral tuberculous lymphadenitis the author has found the supraclavicular and axillary lymph nodes affected only one third as often as the upper cervical group. This form also showed a tendency to appear later in life, with a maximal incidence at the age of 15, compared with nine years in the latter type. More than half of this group showed x-ray evidence of intrathoracic tuberculosis, which usually took the so-called childhood form, with one or more small foci in the periphery of the lung and massive enlargement of the tracheobronchial lymph nodes. Calcification was usually present in these lesions. Much less commonly the associated pulmonary disease was of the adult type, with extensive cavitation and fibrosis and no mediastinal adenopathy. By reason of its pulmonary origin and the associated tracheobronchial disease, tuberculosis of supraclavicular and axillary lymph nodes has a significance quite different from that in the nodes of the upper part of the neck. It should, of course, be remembered that tuberculosis tends to spread from one group of lymph nodes to the next, by either normal or retrograde paths. Those unusual cases in which tuberculosis involves simultaneously the upper cervical and tracheobronchial lymph nodes, between which there is no direct anatomic connection, are probably due to concomitant infection of both the upper and the lower parts of the respiratory tract.

Indian Medical Gazette, Calcutta

72: 585-648 (Oct.) 1937

Circumscribed Outbreak of Typhus-like Fever in Muzaffargarh District, Southwestern Punjab: Note. M. Yacob.—p. 585.
Anemia of Pregnancy. S. Mitra.—p. 586.
Structural Changes in Parathyroids in Vitamin Deficiency. R. K. Pal.—p. 593.
*Lead Poisoning from Lining of Copper or Brass Cooking Utensils: Report of Case. M. Sein.—p. 595.
Chemistry of Calcium in Tuberculosis. S. K. Sen.—p. 598.
Relation of Systemic Blood Pressure to Intra-Ocular Pressure. J. N. Jaswal.—p. 602.
Transplantation of Ureters into Pelvic Colon. K. V. Ramana Rao.—p. 603.
Guinea Worm. H. S. Trewn.—p. 606.
Spinal Anesthesia. S. A. Malik.—p. 609.
*Occurrence of Weil's Disease in India. B. M. Das Gupta and R. N. Chopra.—p. 610.

Lead Poisoning from Cooking Utensils.—Sein reports a case in which a person bought new metal cooking pots in March 1936 and, having had them lined (with tin and lead), used them from April. In May attacks of colic, abdominal distention and diarrhea began and these became worse in June. He recovered from the attack, possibly because the lead from the lining had been removed and he had by then excreted the poison from his system. The symptoms recurred with greater severity about the end of September after more utensils were lined. He then had been using the newly lined cooking pots for a couple of weeks. This time the attack was acute and his admission to the hospital apparently saved him from a much worse attack. From the fact that when the patient left the hospital there was little left of the lining of the pots it could be surmised that a large portion must have become dissolved in the articles cooked within a couple of weeks of beginning to use these pots—hence the acuteness and the severity of the symptoms. The fact that the patient was living largely on milk probably prevented him from suffering complications, as he was unwittingly administering to himself the antidote with the poison. With regard to lead poisoning, no systematic study has been made of its incidence and prevention as an occupational disease. It is suggested that an organized inquiry might be held into the question of lead poisoning of the workmen engaged in lining these pots and also of the persons who use them for cooking. It is possible that legislation might be found advisable to prevent such poisoning.

Weil's Disease in India.—The workers who have successfully cultivated Leptospira from the blood of patients with Weil's disease are inclined to the view that successful results are obtained only when the blood cultures are taken within the first seven days of illness. Das Gupta and Chopra obtained a positive blood culture as late as the ninth day (from what they believe to be the first case in India), but the guinea pigs inoculated at the same time proved refractory to infection. Although found in fairly large numbers in the urine, the leptospirae were always immobile and most of them showed varying degrees of degeneration. This is probably due to the presence of plenty of bile (which has a lytic action on Leptospira) still present in the urine.

Lancet, London

2: 835-890 (Oct. 9) 1937

Injection Treatment of Inguinal Hernia: Report on 100 Cases. A. E. Porritt.—p. 835.
*Gold Treatment of Arthritis: Review of 900 Cases. S. J. Hartfall, H. G. Garland and W. Goldie.—p. 838.
Absorption and Excretion of Estrone by Human Organism. T. Kemp and K. Pedersen-Bjergaard.—p. 842.
Transformation of Male Sex Hormones into a Substance with Action of Female Hormone. E. Steinach and H. Kun.—p. 845.
*Macroscopic Agglutination Test for Diagnosis of Weil's Disease. J. Smith and W. J. Tulloch.—p. 846.
Control of Postoperative Urinary Retention with Doryl. R. Officer and J. C. Stewart.—p. 850.

Gold Salts in Treatment of Arthritis.—Hartfall and his colleagues have employed chrysotherapy in the treatment of 900 cases of arthritis, 750 of which were of rheumatoid arthritis. They maintain that preparations of gold constitute the best single form of treatment in rheumatoid arthritis. They are still unable to predict toxic reactions, although they are at present investigating a patch test which appears to be giving promising results. The factors on which toxic reactions depend are still unknown, but from their experience they feel justified in drawing the following tentative conclusions: Certain individuals undoubtedly show an idiosyncrasy to gold salts, developing multiple reactions after small doses, and these patients are presumably unsuitable for treatment. In others there are no doubt several factors; dosage is of some importance. The maximal single dose should not be more than 0.1 Gm. and a course of injections should not consist of more than 1 Gm. At the same time larger doses produce even more striking results. It is probable that some preparations of gold are more toxic than others, but their toxicity does not appear to be dependent on the route of injection. Age and sex, severity and duration of the disease appear to have no bearing on the frequency of reactions, nor has any relationship been found between the blood sedimentation rate and the development of toxic reactions. There are a few real contraindications to treatment with gold salts; any history of previous purpura or agranulocytosis appears to be an absolute contraindication, as is gross renal or hepatic disease. Rheumatoid arthritis, if seen in its early stages, can be cured by gold salts, and there are few cases that cannot be improved to some extent. Any acute nontraumatic monarticular arthritis should be regarded as the possible forerunner of widespread and severe rheumatoid arthritis. Every patient should have at least two courses of injections, and a persistently raised blood sedimentation rate is an indication for further treatment with gold salts.

Agglutination Test in Weil's Disease.—Smith and Tulloch point out that in view of the experience of one of them (Tulloch) when investigating the agglutination reactions of separated bacterial flagella it seemed probable that, although cultures of Leptospira do not show much turbidity before exposure to antibodies, they could, on such exposure under suitable conditions, produce floccules that would be seen easily. It is possible to prepare a suspension of bacterial flagella which is virtually transparent although it contains enormous numbers of these structures. When such transparent flagellar suspensions are exposed to their appropriate (antiflagellar) serum, floccules are formed which can be seen by the naked eye, if indirect illumination is employed. In view of what is known concerning the mechanism of agglutination, it seemed highly probable that once the leptospirae were sensitized by their appropriate antibody they would not exhibit the same tendency to fragmentation on exposure to heat as they do in the unsensitized state. Should this be so, incubation at a temperature between 30 and 37 C.—sensitizing incubation—could be followed by a short exposure to 55 C.—flocculating incubation—in order that the rapidity of the reaction might be increased. Actually this proved to be the case. Comparative tests were made with the Schüffner procedure and the macroscopic agglutination method and the results for the two were remarkably alike. The lytic action of the Schüffner technic is not complete and apparently interferes in no way with the interpretation of the macroscopic test. The end titer of an immune serum is somewhat difficult to determine without considerable practice when the darkfield method is employed, but no particular dubiety occurs in connection with the interpretation of the macroscopic method. The ease with which macroscopic tests can be carried out and interpreted demands special emphasis, since this makes possible a much wider application of serologic methods to the study of leptospirosis, both in man and in rodents.

Medical Journal of Australia, Sydney

2: 543-584 (Oct. 2) 1937

Galen, the Medical Dictator: His Life and Influence on Progress of Medicine. L. Cowlishaw.—p. 543.
*Schizophrenia and Its Treatment by Insulin and "Cardiazol." R. S. Ellery.—p. 552.
Anatomy of Capsular Vascular Disease. A. A. Abbie.—p. 564.
*Use of Adrenalin in Vaginal Plastic Operations: Note. R. I. Furber and A. R. H. Duggan.—p. 568.

2: 585-630 (Oct. 9) 1937

Common Problems in General Practice. G. W. Ashton.—p. 585.
Sydenham's Chorea: Its Course and Relationship to Rheumatic Fever. S. Williams.—p. 590.
Doctors and the Law. D. M. Morton.—p. 593.
Effect of Drinking Water on Lead Poisoning in Experimental Animals. G. Croll.—p. 598.
A Voyage from Plymouth to Adelaide in the Forties: Impressions of a Ship's Surgeon. K. M. Brown.—p. 600.
Alterations to Footwear. N. Little.—p. 603.

Schizophrenia and Its Treatment by Insulin and Metrazol.—Ellery discusses the many methods of previous empirical treatment of schizophrenia and concludes that the whole point about the empirical organic procedures of the past is that, while it is better to apply treatment which will achieve sporadic success and a certain amelioration of symptoms than to stand by resignedly, not one of the methods is capable of giving results consistently better than those which are liable to occur spontaneously, if one accepts the dictum that such remissions occur in approximately 20 per cent of unselected schizophrenic patients. Complete details are given of insulin shock (Sakel) and metrazol convulsion (Meduna) therapy. To the unfamiliar observer hypoglycemic shock therapy may look particularly dangerous and somewhat cruel. However, in the hands of a competent physician who has familiarized himself with all aspects of the treatment, the dangers are often more apparent than real. From the patients' point of view the treatment is neither perilous nor painful. Amnesia prevents them from remembering any of their more distressing symptoms. Almost invariably patients gain weight and begin to feel more physically fit. This, together with the return of lucidity, more than compensates for any initial discomfort they may have experienced. By the proper use of the insulin shock treatment one is now able to anticipate some 70 to 80 per cent full remissions in schizophrenic patients whose illness is of less than six months' duration, and approximately 60 per cent of full remissions in those whose mental disorder has persisted for not more than eighteen months at the time of treatment. For patients who have been ill for longer than eighteen months the chance of achieving a remission diminishes rapidly as the length of the illness increases and as defect symptoms are manifest; but from the not altogether negligible number who do seem to recover, nearly 50 per cent show varying signs of improvement. With metrazol therapy in 50 per cent of unselected cases, in which the length of illness has varied from one week to ten years, a good remission has been obtained. In especially early cases, before the onset of permanent symptoms of mental deterioration, the reaction to this form of treatment has been most favorable, and Meduna states that he has brought about a remission in 80 per cent of such cases. Reviewing his results in individual cases, he finds that a good response may be anticipated in schizophrenic patients in whom symptoms have not persisted for more than four years. He has failed absolutely to produce any good results in patients whose symptoms have persisted for a longer time. The best responses to metrazol have been achieved in the catatonic and hebephrenic types of schizophrenia. Until results are published Meduna's figures must stand, a challenge to the modern psychiatrist confronted with the schizophrenic problem. Conclusions are drawn from both methods of treatment. The epileptic state is common to the two procedures, and a tentative suggestion is put forth that this may act by changing the biochemical milieu of the human organism in a beneficial way not yet understood, or that it may act merely as a shock, serving by its very intensity to bring the patient into a state of dependence, so that he can obtain benefit from the individual attention of those around him, together with common sense psychotherapy consciously or unconsciously applied by the physician.

Epinephrine in Vaginal Plastic Operations.—It has been the custom of Furber for eighteen years to inject into the superficial tissues a 1:350,000 solution of epinephrine hydrochloride in physiologic solution of sodium chloride when doing vaginal plastic operations. The procedure eliminates the continuous drip method, maintains a clear field (which favors greater accuracy of dissecting and suturing) and diminishes loss of blood. The original method of the continuous drip allowed a large volume of saline solution to flow over the operative field, carrying away an unknown and often large quantity of blood from the dissected tissues. The solution spreads in a natural plane of cleavage, and dissection is greatly facilitated. For a cystocele of average size about 10 cc. of solution is required, and a similar amount for an average cervical repair. It has been suggested that reactionary hemorrhage and delayed union or malunion of the tissues might follow the use of such a method. Furber and Duggan have watched carefully and have never experienced the former, and they have been unable to observe any change in the uniting powers of the tissues in several hundred cases. Their share of secondary hemorrhages has been no more than that experienced by most gynecologic surgeons.

South African Medical Journal, Cape Town

11: 663-706 (Oct. 9) 1937

Visceral Disharmony. E. G. Dru Drury.—p. 665.
Stokes-Adams Syndrome. S. de Boer.—p. 674.
Medicine in the Old Testament. L. P. Bosman.—p. 678.

Journal of Oriental Med., Dairen, S. Manchuria

27: 37-100 (Oct.) 1937. Partial Index

Microscopic Studies on Innervation of the Lung. S. Hayasi.—p. 37.
Adsorption of Specific Precipitable Substance in Blood: Part III. Experiments with Antihuman Hemoglobin Precipitin. Wang Shih-Kong.—p. 80.
Antigenicity of Diphtheria Toxoid Administered in Different Forms. K. Manako.—p. 82.
A New Culture Medium for Type Differentiation of Diphtheria Bacilli. G. Isiyama.—p. 83.
Thrombophlebitis Occurring in Typhus and Typhoid: Three Cases. T. Matuura, M. Sugiura and S. Egi.—p. 89.
Typhoid Accompanied by Noma: Case. S. Egi.—p. 90.
Ascorbic Acid Value of Vegetables and Fruits in Dairen. T. Shidoh and M. Kobayashi.—p. 91.
Seasonal Changes of Vitamin C in Vegetables. E. Tanabe.—p. 93.
Appendicitis with Transposition of Viscera: Two Cases. S. Baba, T. Shoji and R. Sumigawa.—p. 96.

Presse Médicale, Paris

45: 1555-1578 (Nov. 6) 1937

*Vascular Reactions of Brain in Course of Solid and Gaseous Embolisms: Experimental Study on Cerebral Vascular Spasms. M. Villaret, R. Cachera and R. Fauvert.—p. 1555.
*Method of Roentgenographic Sections: Tomography or Planigraphy Applied to Cancer of Larynx. G. Canuyt and Gunsett.—p. 1559.
Effects of Contrast Medium in Roentgenologic Exploration of Viscera. E. L. Lanari, M. E. Jorg and J. A. Aguirre.—p. 1562.
Technic of Metallic Osteosynthesis Applicable in Fractures of Leg and of Long Bones. P. Alglave.—p.1566.
Congenital Pachyonychia with Keratodermia and Disseminated Keratoses of Skin and of Mucous Membranes. A. Touraine.—p. 1569.
Operative Indications and Technic of Intervention in Fractures of Lumbar Transverse Processes. R. Dupont and H. Evrard.—p. 1573.
*Pneumographic Study of Tumors of Lateral Ventricle. H. Askenasy.—p. 1576.

Study on Vascular Reactions of Brain.—Studies made by Villaret and his associates demonstrate the oppositoin that exists between intense reactions in the arterioles of the pia mater in case of solid embolism and the complete absence of vasomotor response at the time of gaseous embolism in the same vessels. Their experiences on solid cerebral embolism make it possible for them to make evident in an objective manner a phenomenon the significance of which has often been invoked and denied in neurology but the existence of which, in the form of spasm of the cerebral arteries, had never been verified. Henceforth, its authenticity cannot be doubted. However, in view of the short duration of the observations and of the absence of anatomic controls, the authors regard all physiopathologic deductions on this subject as premature. On the other hand, they stress the importance of their observations for the physiologic problem of cerebral vasomotoricity. They brought the proof of the possibility of producing spasms of the cerebral vessels by direct endovascular excitation, just as Riser had emphasized the existence of spasms by exogenic, either mechanical or electrical, irritation. The experimental gaseous embolism of the brain demonstrated, on the other hand, the complete indifference of the arteriolar walls to the embolized air bubbles. The authors were never able to demonstrate cerebral vasoconstriction in these conditions. The hypothesis of vascular spasms, often invoked recently to explain the nervous accidents of gaseous embolisms, do not seem to be well founded. The authors further state that they were able to demonstrate in the same animal, first, the complete inertia of an arteriole of the pia mater to a gaseous embolism and then the spasmodic reaction of the same vessel to solid cerebral embolism; namely, to the injection of pulverized pumice stone. However, these investigations nevertheless make apparent the possibility of an essential phenomenon in the course of gaseous embolism; namely, the circulatory arrest. Provoked by the air, which acts like a tampon and interrupts the circulation of the blood, this arrest elicits in the involved arterial region a temporary ischemia which, if prolonged, may no doubt cause grave alterations in elements as sensitive as the nerve cells. The authors think that the local mechanism of accidents resulting from gaseous embolism of the brain is a cerebral ischemia, which in turn is elicited by gaseous obstruction.

Tomography Applied to Cancer of Larynx.—Canuyt and Gunsett point out that the method of roentgenologic sections (tomography), which has been found helpful in the diagnosis of pulmonary disorders, is helpful also for the examination of the larynx. It permits a comparison of the right and left side of the larynx. In applying it in pathologic disorders of the larynx and particularly in laryngeal cancer, the authors obtained encouraging results. No other method gave as precise results as did tomography, and they conclude that this method represents a considerable progress in the study of the localization and extension of cancerous lesions of the larynx.

Pneumographic Study of Tumors of Lateral Ventricle.—Askenasy points out that the ventriculography with injection of air, that is, the pneumography of the cerebral ventricles, is chiefly the work of Dandy and that this method has greatly modified the diagnosis, therapy and prognosis of the tumors of the lateral ventricle. On the basis of his own experience with this method, he says that from the characteristics of the ventriculogram it seems possible to distinguish the primary intraventricular tumors from tumors that have invaded the lateral ventricle secondarily. In the primary intraventricular tumors it is necessary to differentiate between the neoplasms situated at a distance from the interventricular foramen and those located near this foramen. The first ones determine the exclusion of that part of the ventricle which is located back of the tumor and this closed cavity is the site of a considerable dilatation. The second type of tumors, those located near the interventricular foramen, elicit a hydrocephalus that extends over the entire ventricle of the diseased side. These, however, do not generally cause a marked deformation or displacement of the lateral ventricle. In extraventricular tumors, which cause an external stenosis of the interventricular foramen (meningiomas of the small wing of the sphenoid, temporal gliomas and so on), the ventricular hydrocephalus is located on the healthy side, whereas the diseased lateral ventricle is collapsed by the cerebral edema. The secondary intraventricular neoplasms do not cause interruption of continuity in the image of the ventricle of the diseased side. The external wall of the ventricle is deformed by a mass coming from outside and the hydrocephalus, if it exists, is always much less marked than in the case of primary intraventricular tumor.

Gazzetta Internazionale di Med. e Chir., Naples

47: 643-678 (Oct. 31) 1937

*Renal Elimination of Bacteria Injected in Blood. A. Ligas.—p. 643.
Ambulant Treatment in Cutaneous Diseases. M. Agostini.—p. 655.

Renal Elimination of Bacteria Injected in Blood.—Ligas experimented on rabbits inoculated with bacterial broth cultures directly in the left ventricle or in the marginal vein of the ear. The bacteria administered were staphylococci, streptococci, pneumococci and bacilli of the coli and paracoli groups, in doses of about 1,000 bacteria for each kilogram of body weight. The urine was withdrawn by puncture of the bladder at intervals which varied from three minutes to ninety-six hours after inoculation. The sterile quality of the urine was verified before the inoculation. Cultures were made from the urine, bile, blood, kidney and spleen of the animals that died spontaneously or were killed. The different bacteria were identified. The author concludes that the kidney eliminates bacteria as though it were an inert body for the first forty-five minutes. When the bacteria are in contact with the kidney for more than forty-five minutes, anatomic lesions develop in the structure. The time of elimination varies with different bacteria. The colon bacillus and the streptococcus are eliminated in the urine three minutes and forty-five minutes, respectively, after inoculation in the blood. The passage of bacteria through the kidney induces biologic reactions of a physiologic type if bacteria are in contact with the kidney for a short time and of a pathologic type if the contact is prolonged.

Giornale di Clinica Medica, Parma

18: 1303-1400 (Oct. 30) 1937

Indicanuria in Nephropathies. L. Supino.—p. 1303.
*Inflammatory Reactions in Course of Bronchopneumonia in Leukemia. M. Dreyfuss.—p. 1311.
Experimental Osteomyelitis from Colon Bacillus. L. Mezzana.—p. 1342.
Hepatomegaly, a Sequel to Undulant Fever: Clinical Study. G. Drei.—p. 1368.

Inflammatory Reactions of Lung in Leukemia.—Dreyfuss made a microscopic study of the lung in four cases of bronchopneumonia in the course of leukemia. In one case of fibrous bronchopneumonia, complicated by the presence of many micro-abscesses, degenerated polymorphonuclear leukocytes predominated in the intra-alveolar exudates. There were a few lymphocytes and histiocytes. In the remaining three cases there was a leukemic reaction with proliferation of leukemic cells and histiocytes and the presence of a few polymorphonuclear granulocytes or no granulocytes at all. According to the author, the mesenchyma of the lung is frequently and intensely involved in the process of leukemia. It reacts by means of proliferations around the vessels and bronchi and at the nodules and interalveolar septums. The cellular picture of bronchopneumonia in leukemia depends on the functional condition of the organs concerned with the defense of the cells. When the organism can still fulfil the functions of granulopoiesis, the lung reacts to the stimulation of the inflammation by the production of exudates which are rich in polymorphonucleated leukocytes.

If the activity of the granulopoietic functions is diminished, the reticulo-endothelial system of the lung reacts by the production of leukemic cells and histiocytes, which form the interalveolar exudates in cases of this nature. If leukemic metaplasia is not advanced and if it is still reversible, the lung will show a microscopic picture of histiocytic alveolitis. If the functions of the reticulo-endothelial system of the lung are disturbed by the intensity of the leukemic metaplasia, immature leukemic cells prevail in the exudates, and sometimes they are the only cells which form the interalveolar exudates. Grave leukemic metaplasia inhibits the organic cellular defenses with consequent paralysis of the reticulo-endothelial system of the lung and absence of local cellular reaction.

Riforma Medica, Naples

53: 1437-1468 (Oct. 9) 1937

*Autohemotherapy in Paralysis of Ocular Muscles. R. Campos.—p. 1439.
*Experiments on Detoxicating Action of Aminoacetic Acid for Arsphenamine. A. Versari.—p. 1443.
Pure Alexia: Case. G. Palomba.—p. 1445.

Autohemotherapy in Paralysis of Ocular Muscles.—Campos reports satisfactory results from autohemotherapy in two cases of paralysis of the ocular muscles following hemiplegia of nuclear origin. The technic is as follows: Twenty cubic centimeters of blood is taken from a vein of the patient's arm and immediately reinjected at the gluteal region, which is then massaged for some time. The injections are given at intervals of two days alternately on each side of the gluteal region up to ten injections. The condition of the author's patient was slowly but progressively aggravated during the first month before he resorted to autohemotherapy. The latter induced in both cases complete regression of the symptoms and functional reestablishment in about one month. The treatment is simple and harmless.

Detoxicating Action of Aminoacetic Acid for Arsphenamine.—Versari experimented on two groups of rabbits, which were given 0.25 and 0.35 Gm., respectively, for each kilogram of body weight, of arsphenamine dissolved in 5 cc. of a 4 per cent solution of aminoacetic acid in distilled water. In the first group the largest number of animals survived the experiment and showed no organic alterations when they were killed, three months after the experiment. Of the animals that died, death occurred between the first and seventh days. All the control animals in the group which were given the same amount of arsphenamine without any aminoacetic acid died during the first two days of the experiment. In the second group, all the animals but one died between the fourth and fourteenth days of the experiments. The controls in the group died within seven days. The author concludes that the toxicity of arsphenamine is greatly diminished if aminoacetic acid is simultaneously administered. He believes that it synthesizes arsphenamine into a new product that is eliminated from the organism later on in the course of the reaction.

Prensa Médica Argentina, Buenos Aires

24: 2045-2090 (Oct. 27) 1937

Regression and Reabsorption of Cancer Tumors by Hydrolysates of Striate Muscle. A. H. Roffo.—p. 2048.
Foreign Bodies in Duodenum: Clinical Study. H. Taubenschlag.—p. 2061.
*Intolerance to Emetine with Skin Lesions. R. Lorenzo and Matilde Portnoy.—p. 2065.
Biologic Treatment of Prolonged Endocarditis with Streptococcus Viridans. L. L. Resio and I. Berendorf.—p. 2071.
Epithelioma of Vulva: Cases. P. Ronchi, M. Mazza and J. J. Courtis.—p. 2073.

Intolerance to Emetine with Development of Cutaneous Lesions.—Lorenzo and Portnoy report a case of amebiasis. Treatment with enterovioform resulted in the disappearance of Amoeba histolytica cysts and paracysts from the feces. An injection of 0.03 Gm. of emetine hydrochloride was given each day for five consecutive days. The second injection was followed by a cutaneous reaction of the allergic type with the appearance of local eruption and an infiltrating reaction at the point of injection. The third injection was followed by a reaction of an anaphylactic type with shock and generalization of the eruption all over the body. The fourth and fifth injections caused intensification of the eruption. The reaction subsided on discontinuation of the emetine injections and on administration of calcium and epinephrine. After a period of rest, three series of emetine hydrochloride injections were administered. Each series consisted of two injections of 0.03 Gm. of emetine hydrochloride, which were given for two consecutive days and followed by an interval of rest. The skin reaction was less severe after the second and third series of injections and did not take place after the fourth series. The authors believe that their case was one of allergy of the type of cutaneous anaphylaxis which was due to repeated organic absorption of disintegrated bacterial matter.

Fortschritte der Therapie, Leipzig

13: 537-592 (Oct.) 1937. Partial Index

*Treatment of Agranulocytosis. H.-E. Bock.—p. 537.
New Methods for Treatment of Gonorrhea. C. Fischer.—p. 553
Bee Venom as Therapeutic. R. Schwab.—p. 560.
Intestinal Extracts in Allergic Diseases. L. Adelsberger.—p. 568.

Treatment of Agranulocytosis.—Bock points out that heretofore agranulocytic conditions have been treated with roentgen irritation of the long bones, repeated injections of nucleotide and profuse blood transfusions. However, in acute cases of agranulocytosis these measures rarely prove sufficient for the compensation of the lack of granulocytes during the first four severe days. In an extremely severe case of agranulocytosis, transfusions with blood of a patient who had leukemia were made. This was possible because a person of the same blood group who had myeloid leukemia was available as a donor. In this connection the author points out that Schittenhelm before him had resorted to the transfusion of the blood of a patient with untreated chronic myeloid leukemia in a case of agranulocytosis. He thinks that Schittenhelm was the first who proved that severe agranulocytosis could be successfully treated with leukemic blood. The difference between Schittenhelm's case and the one described here was that Schittenhelm gave only a single transfusion of leukemic blood, whereas in the reported case fourteen transfusions were given. In the latter case of agranulocytosis, in which angina, necrosis of the gums, pneumonia and later on abscess of the thigh developed, the destruction of leukocytes was extremely severe. The quantity of leukocytes transmitted to the agranulocytic patient in the course of the fourteen transfusions was equivalent to the quantity that would have been provided by 250 transfusions of ordinary blood. The author admits that not all patients with agranulocytosis require such enormous amounts of leukocytes nor does he think that all require leukemic blood. Regarding the leukemic donor, he says that withdrawal of blood and immediate replacement by normal blood are not harmful for a patient with chronic leukemic myelosis but may even exert a beneficial influence.

Klinische Wochenschrift, Berlin

16: 1521-1560 (Oct. 30) 1937. Partial Index

Sympathetic Optical System. E. Scharrer.—p. 1521.
Function and Functional Tests of Lung. G. Zaeper.—p. 1523.
*Clinical Aspects and Pathogenesis of Ketonemic Vomiting in Diabetic Children. H. Hungerland.—p. 1526.
How to Furnish Morphologic Proof for Corticotropic Hyperpituitarism. E. J. Kraus.—p. 1528.
Immunizing Efficacy in Malignant Diphtheria. H. Baar and N. Kovács.—p. 1532.
Acute Symmetrical Cutaneous Gangrene in Scarlet Fever. H. Klan.—p. 1538.
Influence of Cevitamic Acid on Blood Pressure. M. Kasahara and R. Kawamura.—p. 1543.

Ketonemic Vomiting in Diabetic Children.—Hungerland reviews the literature on ketonemic vomiting and reports a case of his own observation. A boy, aged 5, had attacks of vomiting and the examination revealed a diabetic coma. The author points out that there are contradicting theories about the genesis of ketonemic vomiting. He cites Schiff's remark about ketosis. Schiff maintained that ketosis may be caused by an excessive production of insulin but also by a blockage or exhaustion of the carbohydrate depots. On the basis of this theory, Schiff rejected the administration of insulin as dangerous in cases of ketonemic vomiting. Other authors, Fanconi among them, found insulin helpful. To be sure, Fanconi admits that during the first period of acetonemic vomiting insulin should not be given alone but together with carbohydrates. The author thinks that Fanconi's patients had diabetes mellitus. In this

connection he discusses the symptomatology of diabetic coma, particularly the occurrence of vomiting, and points out that vomiting is more frequent in children with ketonuria than in adults. Vomiting seems to occur no matter of what origin the ketonuria may be, whether caused by hyperinsulinism or by hypo-insulinism. Deficiency of carbohydrates, excess of insulin or shortage of insulin all may lead to a disturbance in the carbohydrate metabolism, which results in ketonuria. Vomiting in children with diabetic coma is only a special form of ketonemic vomiting. In the conclusion the author directs attention to the fact that ketonemic vomiting develops only in a certain type of children but that in this type of children any of the aforementioned metabolic disturbances may elicit ketonemic vomiting. As regards the treatment the author says that, depending on the genesis of the disorder, carbohydrates as well as insulin, or both, may be required.

Zeitschrift f. d. ges. experimentelle Medizin, Berlin

101: 307-450 (Sept. 20) 1937. Partial Index

Digestion Leukocytosis and Cerebral Regulation of Blood Picture. H. Regelsberger and W. Kinkelin.—p. 307.
*Question of Postoperative Cerebral Vascular Shock. Charlotte Frisch and H. Hoff.—p. 335.
*Alteration of Muscle Chronaxia by Sympathetic Influences. J. Weiser.—p. 339.
Saturated Stearins in Ox Bile. R. Pertzborn.—p. 350.
Epilepsy Produced by Pyrrole. P. Rezek.—p. 359.
Origin of Hyperglycemia in Duodenal Tolerance Test. E. Lauschner.—p. 365.
*Relation of Most Important Vitamins to Carbohydrate Metabolism. H. Schroeder.—p. 373.

Postoperative Cerebral Vascular Shock.—Frisch and Hoff say that Hering demonstrated that in case of irritation at the site of the division of the common carotid artery a noticeable decrease in blood pressure takes place by way of the nerve of the carotid sinus. They themselves were interested in the question whether this process can be influenced by the pressure conditions within the cranium. They found that the carotid sinus reflex remains unchanged when the cranium and dura are opened or when hypertension is induced by kaolin. However, this reflex disappears if a rather large amount of blood (30 cc.) is withdrawn from a cerebral vessel, whereas it remains unchanged in the case of withdrawal of a tenfold amount of blood from the peripheral vessels. In some instances there even develops a paradoxical reaction (slight increase in blood pressure). This reaction is caused by a central shock of the vasomotor centers. Thus it has been demonstrated that the carotid sinus reflex is dependent on a central regulating factor.

Alteration of Muscle Chronaxia by Sympathetic Influences.—Weiser shows that the convulsions of tetany are not sufficiently explained by the calcium theory. He thinks that the regular concurrence of trophic and sympathetic disturbances and the dependence of tonus, spasm and chronaxia on central influences suggest relations of the sympathetic disturbances and spasms to the regulatory centers in the brain stem. The demonstration of hypersensitivity does not fully explain the irritation of the muscle in tetany. Attention should be given also to chronaxia, for it is increased before the convulsion and has diagnostic significance. The chronaxia is increased in case of catheterization of the stomach; besides the hyperventilation at the onset of the examination and the possible alkalosis by the administration of acid in the further course, the mere touching of the gastric wall has an important part in the alteration of the conditions of irritation in the muscle, which finally may become manifest in an actual spasm. The alteration must be explained as a reflex action. Irritation of the stump of the vagus leads in the animal experiment to a prolongation of the muscle chronaxia. This increase in the muscle chronaxia can be suppressed by the previous administration of atropine. In patients with signs of a sympathetic neurosis and in patients with hepatic disorders, chronaxia is unstable; it has a tendency to increase or is constantly increased. On the basis of clinical signs and of experimental observations, prolonged chronaxia is regarded as a sign of vagotonia. In exophthalmic goiter, the chronaxia values are low.

Relations of Vitamins to Carbohydrate Metabolism.—Schroeder investigated the relations of the most important vitamins to the carbohydrate metabolism and particularly the action of the isolated vitamins on the disordered metabolism in diabetes mellitus. He says that a direct connection between diabetes mellitus and vitamin A is unknown. Carotene as well as vitamin A is found in the blood serum of diabetic patients, but during diabetic coma they disappeared from the blood. In view of the antagonism between vitamin A and thyroid secretion, it may be assumed that the carbohydrate metabolism is indirectly influenced by vitamin A. Vitamin B_1 has no effect on the blood sugar content. Nevertheless, a slight increase in tolerance for dextrose could be produced in diabetic patients by means of vitamin B_1. In this connection the author points out that the insulin-like action of yeast, which has been observed by several investigators, is probably due to the presence of lactoflavin, for the intravenous injection of lactoflavin reduces the blood sugar content of diabetic patients by 20 or 30 per cent. He further reports investigations on the action of vitamin B_1 and of lactoflavin on the growth and the glycogen content of various organs of rats which had B avitaminosis. Whereas the glycogen content of muscles and heart remain practically constant during the B avitaminosis, the glycogen content of the liver decreases. However, the weight as well as the glycogen content of the liver increases in these rats with B avitaminosis, as soon as pure vitamin B_1 is administered by subcutaneous injection. If a mixture of vitamin B_1 and of lactoflavin is given, the result is the same. The increase in weight that can be produced by the administration of vitamin B_1 can be inhibited by the simultaneous administration of dextrose. This can be explained by the dependence of the vitamin B_1 requirements on the carbohydrate metabolism. Studies on the modification of the carbohydrate metabolism by vitamin C revealed that the injection of 300 mg. of cevitamic acid regularly reduces the blood sugar of normal persons. This modification of the blood sugar content is lacking in patients with increased vitamin C requirements. The author suggests that the action of vitamin C on the blood sugar of healthy persons might be explained by the observed inhibition of the insulin antagonist thyroxine. However, this inhibition must take place indirectly, for a direct modification of the action of thyroxine by cevitamic acid proved impossible in the experiment. In elimination experiments following oral tolerance tests with 300 mg. of cevitamic acid daily, it could be proved that patients with diabetes mellitus have greater vitamin C requirements than have normal persons. Observations on the blood sugar prove that the action of insulin is increased by cevitamic acid. That vitamin D is involved in carbohydrate metabolism is proved by the fact that ultraviolet irradiation effects a reduction in the sugar content of blood and urine of diabetic patients.

Wiener klinische Wochenschrift, Vienna

50: 1443-1474 (Oct. 22) 1937. Partial Index

Biologic Foundations of Problem of Male Climacteric: Pathogenesis and Glandular Therapy of Hypertrophy of Prostate. L. Moszkowicz.—p. 1444.
Intravital Microscopy of Unstained and of Vitally Stained Mucous Membrane. J. Pick.—p. 1449.
Colloid Chemical Processes in Artificial and Spontaneous Thrombosis. E. Friedländer.—p. 1451.
*Problem of Anemia After Gastric Resection. M. D. Manizade.—p. 1455.
Wide Aorta of Congenital Origin. S. Kreuzfuchs.—p. 1458.
Chylothorax: Case. M. Szajna.—p. 1460.

Anemia After Gastric Resection.—Manizade points out that progress in research on anemia has proved the importance of gastric digestion for the blood and thus has corroborated the objections of internists to gastric resections. It has been asserted that the so-called resection anemias may develop from five to ten years after the intervention. In order to determine the incidence of anemia after gastric resection, the author examined the blood of forty patients who from five to twelve years previously were subjected to an extensive gastric resection on account of ulcer. In the majority of patients the operation had been performed more than seven years before. The operation and the microscopic examination had demonstrated the existence of a peptic ulcer in all the patients. The patients were of various ages (from 23 to 67 years). Three of them had been operated on according to Billroth's first method, all others according to Billroth's second method. All the resections had been extensive (two thirds resections). The examination

of the blood revealed in thirty-six of the forty patients that the number of erythrocytes was above 4.5 million; the hemoglobin values were likewise normal. Only four of the patients (10 per cent) had an anemic blood picture. Thus it may be concluded that gastric resection in patients with ulcer does not necessarily lead to anemia, although in some cases of gastric resection a predisposition together with secondary digestive disturbances may result in anemia. This possibility makes it necessary before the operation to pay attention to such factors as heredity, constitution, blood picture and gastric juice, and after the operation to watch carefully for the development of digestive disturbances and to institute promptly the proper treatment.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

81: 5387-5502 (Nov. 6) 1937. Partial Index

Correction of Myopia. W. P. C. Zeeman.—p. 5391.
Color of Eyes and Tuberculosis. H. Sandra.—p. 5401.
Chronic Pyodermias. J. A. Folpmers.—p. 5408.
*Clinical Value of Epinephrine Probe Test of Muck. H. A. E. Van Dishoeck.—p. 5415.

Clinical Value of Epinephrine Probe Test.—Van Dishoeck shows that the white streak sign in Muck's epinephrine probe test is positive in a large number of cases in which a disturbance of the sympathetic nervous system exists. However, the clinical value of this test is limited by several factors: 1. By the fact that the white streak sign appears in various and rather frequently occurring disorders; thus the streak sign is not pathognomonic for a definite disease. 2. By the fact that, although the white streak sign appears in a large percentage of cases with sympathetic disturbances, it does not appear in all of them. 3. By the fact that it is elicitable in a considerable number of normal control cases. 4. By the fact that the technic is difficult and requires considerable experience. In unilateral cranial injuries, the white streak sign was often elicitable, usually on the side of the lesion. Because of this, the epinephrine probe test might be of value in the localization of cerebral process. The test is valuable also for the study of the complicated reactions of the nasal mucosa.

Hospitalstidende, Copenhagen

80: 1097-1116 (Oct. 5) 1937

*Nephroptosis: Its Recognition and Treatment. H. Mathiesen.—p. 1097.
Sepsis in the New-Born: Case. P. N. Damm.—p. 1112.

Recognition and Treatment of Nephroptosis.—Mathiesen emphasizes the importance of pyelography, especially vertical pyelography, in cases of possible nephroptosis, and prefers vertical pyelography whenever possible. He says that in suitable cases excellent results can be attained by operative treatment. The indications are grave, constant colic, affecting the patient's ability and desire to work, nephroptosis combined with beginning or developed hydronephrosis or with aberrant blood vessels or cord formation, or complications with nephrolithiasis or recurring pyelitis. The contraindications are advanced age and poor general condition due to causes other than the nephroptosis. The procedure that he now follows is to split the capsule over the lower part of the convex edge of the kidney, bring the kidney into contact with the inner side of the lowest ribs as high as possible and suture the flaps of the capsule there. The outer capsule of the kidney is often gathered about the lower pole with catgut sutures. Occasionally it is necessary to turn the kidney so that the upper pole tips slightly downward, to allow the ureter to pass from the most sloping part of the kidney. When it is difficult to raise the kidney high enough, a strip of fascia lata 1.5 cm. wide is transplanted; after the capsule has been slit over the lower pole, the fascia is sewed fast about this and the ends are passed through an incision in the eleventh intercostal space and sutured to the edges of the wound. He considers the partial decapsulation a particularly important step in nephropexy, as the bloody surface best assures formation of firm adherences between the kidney and its seat. The patient must remain in bed for at least three weeks and must not for some time after discharge do heavy work. Of the author's fifty patients with nephroptosis, twenty-five were treated with nephropexy; of these, twenty are well, two improved and two unchanged and one is dead. In five cases the ptosis was combined with aberrant renal blood vessels. Five cases are reported. The two improved and the two unchanged patients were operated on by other methods than the one described; all patients treated by this method are well.

80: 1117-1144 (Oct. 12) 1937

*Recurring Generalized Osteitis Fibrosa (Recklinghausen) with Parathyroid Adenoma and Diffuse Hyperplasia of Basophil Elements in Anterior Lobe of Pituitary: Case. S. Franck and N. Hjerrild.—p. 1117.
Relation of So-Called Hysterical Reactions to Constitution Type. I. Ostenfeld.—p. 1130.
Paroxysmal Tachycardia with Partial Atrioventricular Block in Child, Aged 8 Years: Case. C. Maarssø.—p. 1140.

Recurring Osteitis Fibrosa.—Franck and Hjerrild state that in this instance of generalized osteitis fibrosa with parathyroid adenoma and diffuse hyperplasia of basophil elements in the anterior lobe of the pituitary there was recurrence about four years after removal of an adenoma of the right parathyroid. Postmortem showed grave changes in different endocrine glands, especially an adenoma of the size of an almond in the left parathyroid, together with diffuse hyperplasia of the basophil cells of the anterior pituitary. The case leads the authors to the opinion that the parathyrotropic hormone of the anterior lobe of the pituitary is probably produced by its basophil elements.

80: 1145-1172 (Oct. 19) 1937

*Investigations on Effect of Extract of Anterior Lobe of Pituitary on Carbohydrate Metabolism in Normal Persons and Diabetic Patients. H. C. A. Lassen and L. Hansen.—p. 1145.
Irregular Glandular Hyperplasia of Endometrium Treated by Excochleation of Uterus. K. H. Köster.—p. 1164.

The Pituitary and Carbohydrate Metabolism.—Lassen and Hansen state that injection of an alkaline extract of the anterior lobe of the pituitary can produce a marked diabetogenic effect both in the normal and in the diabetic organism, together with a considerable increase in ammonia elimination, the latter being presumably an expression of the presence of a ketogenic principle in the extract. The diabetogenic action is doubtful when only small amounts of protein and no carbohydrate are resorbed from the intestine. It is best demonstrated following the ingestion of meals with moderate carbohydrate and protein content. On intake of larger amounts of carbohydrate (about 75 Gm.), either as pure dextrose or in a meal with abundant carbohydrate, the injection of the extract, whether intramuscularly or intravenously, cannot raise the peak of the curve; the diabetogenic effect appears in an increased width of the curve. Finally, the experiments indicate, but do not prove, that injection of extract of the anterior hypophysis can cause a transient fall of the sugar threshold of the kidneys in healthy persons with normal sugar threshold.

Ugeskrift for Læger, Copenhagen

99: 1109-1140 (Oct. 21) 1937

*Electrocoagulation of Lupus Vulgaris in Combination with Other Forms of Local Treatment. V. Genner.—p. 1109.
Postoperative Tetany Treated with A. T. 10: Three Cases. M. Faber.—p. 1118.
Therapeutic Reports from Practice. V. Erlendsson.—p. 1122.
Fandochi. V. Halberg.—p. 1123.

Treatment of Lupus Vulgaris.—The different forms of local treatment of lupus vulgaris at the Finsen Institute are reviewed. Genner says that the Finsen treatment, given by a technically trained and competent personnel, is the main method of treatment and will under these conditions give the best results both as to recovery and cosmetically. Caustic ointment, surgical excision, diathermic excision and electrocoagulation are auxiliary methods. Regard for the cosmetic side must not be carried too far; where light treatment has not resulted in recovery after a reasonable time and recovery is believed possible, recourse must be taken to the more radical adjuvant methods named, the time and the choice to be decided by the physician experienced in treatment of lupus. Electrocoagulation is a supplement that can advantageously be used in connection with light treatment, either as a preliminary treatment or later, in a limited number of cases in which other aids cannot be applied, as in order to destroy superficially isolated well defined nodules. Forty-two cases treated with electrocoagulation and observed for several years are tabulated.